

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
18 November 2004 (18.11.2004)

PCT

(10) International Publication Number  
**WO 2004/099134 A2**

(51) International Patent Classification<sup>7</sup>: **C07D 207/00**

(74) Agent: **BLAKEY, Alison**; Prosidion Ltd., Watlington Road, Oxford OX4 6LT (GB).

(21) International Application Number:

PCT/EP2004/004774

(22) International Filing Date: 5 May 2004 (05.05.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/467,914 5 May 2003 (05.05.2003) US

60/468,014 5 May 2003 (05.05.2003) US

(71) Applicant (for all designated States except US): **PROSIDION LTD.** [GB/GB]; Watlington Road, Oxford OX4 6LT (GB).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **DEMUTH, Hans-Ulrich** [DE/DE]; Hegelstr. 14, 06114 Halle/Saale (DE). **HOFFMANN, Matthias** [DE/DE]; Froebelstr. 1d, 06688 Wengelsdorf (DE). **HOFFMANN, Torsten** [DE/DE]; Koernerstr. 8, 06114 Halle/Saale (DE). **NIESTROJ, André, J.** [DE/DE]; Thälmannplatz 1, 06193 Sennewitz (DE). **SCHILLING, Stephan** [DE/DE]; Läuferweg 4, 06128 Halle/Saale (DE). **HEISER, Ulrich** [DE/DE]; Franz-Schubert-Strasse 5, 06108 Halle/Saale (DE).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: **GLUTAMINYL BASED DP IV-INHIBITORS**

(57) Abstract: The present invention relates dipeptidyl peptidase IV inhibition and, more particularly, relates to glutaminy derivatives, wherein the glutamin residue is bound in a peptide manner to a moiety which imitates the amino acid residue prolin, especially to a nitrogen containing moiety, pharmaceutical compositions containing said compounds, and the use of said compounds in inhibiting dipeptidyl peptidase IV and dipeptidyl peptidase IV-like enzyme activity.

WO 2004/099134 A2

## Glutaminyl based DP IV-inhibitors

### Field of the invention

The present invention relates to the area of dipeptidyl peptidase IV inhibition and, more particularly, relates to glutaminyl derivatives, wherein the glutamin residue is bound in a peptide manner to a moiety which imitates the amino acid residue prolin, especially to a nitrogen containing moiety, pharmaceutical compositions containing said compounds, and the use of said compounds in inhibiting dipeptidyl peptidase IV and dipeptidyl peptidase IV – like enzyme activity.

Further, the present invention concerns the metabolism of the glutamin residue of these glutamin based DP IV inhibitors, which are metabolized and inactivated enzymatically to cyclic compounds by the enzyme glutaminyl cyclase (QC).

It is an aspect of the present invention to provide new DPIV inhibitors, *optionally* in combination with glutaminyl cyclase (QC) inhibitors, which are effective e.g. in treating conditions mediated by inhibition of DPIV and DPIV-like enzymes, pharmaceutical compositions e.g. useful in inhibiting DPIV and DPIV-like enzymes and/or inhibiting QC and QC-like enzymes, and a method of inhibiting said enzyme activities.

Another aspect of the invention relates to a method of treatment, in particular to a method for the treatment of diabetes mellitus, especially non-insulin dependent diabetes (NIDDM) or Type 2 diabetes and conditions associated with diabetes mellitus and to compositions for use in such method.

### Background Art

Dipeptidyl peptidase IV (DPIV) is a serine protease which cleaves N-terminal dipeptides from a peptide chain containing, preferably, a proline residue in the penultimate position. Although the biological role of DPIV in mammalian systems has not been completely established, it is believed to play an important role in



neuropeptide metabolism, T-cell activation, attachment of cancer cells to the endothelium and the entry of HIV into lymphoid cells.

Likewise, it was discovered that DPIV is responsible for inactivating glucagon-like peptide-1 (GLP-1) and glucose-dependent insulintropic peptide also known as gastric-inhibitory peptide (GIP). Since GLP-1 is a major stimulator of pancreatic insulin secretion and has direct beneficial effects on glucose disposal, in WO 97/40832 and US 6,303,661 inhibition of DPIV and DPIV-like enzyme activity was shown to represent an attractive approach e.g. for treating non-insulin-dependent diabetes mellitus (NIDDM).

Dipeptidyl peptidase IV (DPIV) is a post-proline (to a lesser extent post-alanine, post-serine or post-glycine) cleaving serine protease found in various tissues of the body including kidney, liver, and intestine.

It is known that DPIV inhibitors may be useful for the treatment of impaired glucose tolerance and diabetes mellitus (International Patent Application, Publication Number WO 99/61431, Pederson RA et al, Diabetes. 1998 Aug; 47(8):1253-8 and Pauly RP et al, Metabolism 1999 Mar; 48(3):385-9). In particular WO 99/61431 discloses DPIV inhibitors comprising an amino acid residue and a thiazolidine or pyrrolidine group, and salts thereof, especially *L-threo*-isoleucyl thiazolidine, *L-allo*-isoleucyl thiazolidine, *L-threo*-isoleucyl pyrrolidine, *L-allo*-isoleucyl thiazolidine, *L-allo*-isoleucyl pyrrolidine, and salts thereof. In particular PCT/EP 02/07124 discloses DPIV inhibitors comprising an glutaminyl residue and a thiazolidine or pyrrolidine group, and salts thereof, especially glutaminyl thiazolidine and glutaminyl pyrrolidine, and salts thereof.

Further examples for low molecular weight dipeptidyl peptidase IV inhibitors are agents such as tetrahydroisoquinolin-3-carboxamide derivatives, N-substituted 2-cyanopyrroles and -pyrrolidines, N-(N'-substituted glycyl)-2-cyanopyrrolidines, N-(substituted glycyl)-thiazolidines, N-(substituted glycyl)-4-cyanothiazolidines, boronyl inhibitors and cyclopropyl-fused pyrrolidines. Inhibitors of dipeptidyl peptidase IV are described in US 6,011,155; US 6,107,317; US 6,110,949; US 6,124,305; US 6,172,081; WO 99/61431, WO 99/67278, WO 99/67279, DE 198 34 591, WO

97/40832, DE 196 16 486 C 2, WO 95/15309, WO 98/19998, WO 00/07617, WO 99/38501, WO 99/46272, WO 99/38501, WO 01/68603, WO 01/40180, WO 01/81337, WO 01/81304, WO 01/55105, WO 02/02560, WO 01/34594, WO 02/38541 (Japanese), WO 02/083128, WO 03/072556, WO 03/002593, WO 03/000250, WO 03/000180, WO 03/000181, EP 1 258 476, WO 03/002553, WO 03/002531, WO 03/002530, WO 03/004496, WO 03/004498, WO 03/024942, WO 03/024965, WO 03/033524, WO 03/035057, WO 03/035067, WO 03/037327, WO 03/040174, WO 03/045977, WO 03/055881, WO 03/057144, WO 03/057666, WO 03/068748, WO 03/068757, WO 03/082817, WO 03/101449, WO 03/101958, WO 03/104229, WO 03/74500, WO 04/007446, WO 04/007468, WO 04/018467, WO 04/018468, WO 04/018469, WO 04/026822, the teachings of which are herein incorporated by reference in their entirety concerning the inhibitors, their production and their use.

Moreover, WO 03/030946 discloses a gene-therapy for type-2-diabetes by in vivo expression of glucagon-like peptide (GLP-1) and/or glucose dependent insulintropic peptide (GIP), optionally in combination with concurrent administration of dipeptidyl peptidase IV (DPP-IV) inhibitors.

All these documents and applications mentioned in this application shall be deemed to be incorporated herein by reference.

**Definitions:**

The following definitions refer to the whole description and especially to the claims.

The term "alkyl" refers to a saturated, linear or branched, substituted or unsubstituted hydrocarbon group having 1 to 30 carbon atoms, preferably 1 to 20 carbon atoms, more preferably 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 carbon atoms. Concrete examples for an alkyl group comprise methyl ( $-\text{CH}_3$ ), ethyl ( $-\text{C}_2\text{H}_5$ ), n-propyl ( $n\text{-C}_3\text{H}_7$ ), iso-propyl ( $-\text{CH}(\text{CH}_3)_2$ ), n-butyl ( $n\text{-C}_4\text{H}_9$ ), iso-butyl ( $-\text{CH}_2\text{CH}(\text{CH}_3)_2$ ), sek-butyl ( $-\text{CH}(\text{CH}_3)(\text{C}_2\text{H}_5)$ ), tert-butyl ( $-\text{C}(\text{CH}_3)_3$ ), n-amyl ( $n\text{-C}_5\text{H}_{11}$ ), iso-amyl ( $-(\text{CH}_2)_2\text{CH}(\text{CH}_3)_2$ ), neo-amyl ( $-\text{CH}_2\text{C}(\text{CH}_3)_3$ ), tert-amyl ( $-\text{C}(\text{CH}_3)_2(\text{C}_2\text{H}_5)$ ), n-hexyl

(n-C<sub>6</sub>H<sub>13</sub>), 2,2-dimethyl-butyl (-CH<sub>2</sub>C(CH<sub>3</sub>)<sub>2</sub>(C<sub>2</sub>H<sub>5</sub>)), iso-hexyl (-CH<sub>2</sub>)<sub>3</sub>CH(CH<sub>3</sub>)<sub>2</sub>), neo-hexyl (-CH<sub>2</sub>)<sub>2</sub>C(CH<sub>3</sub>)<sub>3</sub>), tert-hexyl (-C(CH<sub>3</sub>)<sub>2</sub>(n-C<sub>3</sub>H<sub>7</sub>)), n-heptyl (n-C<sub>7</sub>H<sub>15</sub>), iso-heptyl (-CH<sub>2</sub>)<sub>4</sub>CH(CH<sub>3</sub>)<sub>2</sub>), neo-heptyl (-CH<sub>2</sub>)<sub>3</sub>C(CH<sub>3</sub>)<sub>3</sub>), tert-heptyl (-C(CH<sub>3</sub>)<sub>2</sub>(n-C<sub>4</sub>H<sub>9</sub>)), n-octyl (n-C<sub>8</sub>H<sub>17</sub>), iso-octyl (-CH<sub>2</sub>)<sub>5</sub>CH(CH<sub>3</sub>)<sub>2</sub>), tert-octyl (-C(CH<sub>3</sub>)<sub>2</sub>(n-C<sub>5</sub>H<sub>11</sub>)), neo-octyl (-CH<sub>2</sub>)<sub>4</sub>C(CH<sub>3</sub>)<sub>3</sub>) or 2,2,4-trimethyl-pentyl (-CH<sub>2</sub>-CH(CH<sub>3</sub>)CH<sub>2</sub>C(CH<sub>3</sub>)<sub>3</sub>) group.

The term "alkenyl" refers to an unsaturated, linear or branched, substituted or unsubstituted hydrocarbon group having at least one double bond having 2 to 30 carbons atoms, preferably 2 to 20 carbon atoms, more preferably 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 carbon atoms. The alkenyl group has one or two or three double bonds, preferably one or two double bonds, and more preferably one double bond. Concrete examples for an alkenyl group comprise vinyl (-CH=CH<sub>2</sub>), allyl (-CH<sub>2</sub>CH=CH<sub>2</sub>), prop-1-enyl (-CH=CHCH<sub>3</sub>), but-1-enyl (-CH=CH(C<sub>2</sub>H<sub>5</sub>)), but-2-en-1-yl (-CH<sub>2</sub>CH=CH(CH<sub>3</sub>)), but-3-en-1-yl (-CH<sub>2</sub>)<sub>2</sub>CH=CH<sub>2</sub>), 2-methyl-prop-2-enyl (-CH<sub>2</sub>C(=CH<sub>2</sub>)(CH<sub>3</sub>)), buta-1,3-dien-1-yl (-CH=CH-CH=CH<sub>2</sub>), 3-methyl-buta-1,3-dienyl (-CH=CH-C(=CH<sub>2</sub>)(CH<sub>3</sub>)), isoprenyl (-CH<sub>2</sub>-CH=C(CH<sub>3</sub>)<sub>2</sub>), or hex-2-enyl (-CH<sub>2</sub>-CH=CH-C<sub>3</sub>H<sub>7</sub>) group.

If the formation of an E configuration or, respectively, a Z configuration of a double bond in an „alkenyl group“ is possible, both the E and Z configuration are comprised in this application.

The term "alkinyl" refers to a unsaturated, linear or branched, substituted or unsubstituted hydrocarbon group having at least one triple bond having 2 to 30 carbons atoms, preferably 2 to 20 carbon atoms, more preferably 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 carbon atoms. The alkinyl group has one or two or three triple bonds, preferably one triple bond. Concrete examples for an alkinyl group comprise acetylenyl (-C≡CH), propargyl (-C≡C-CH<sub>3</sub>), but-1-in-1-yl (-C≡C-C<sub>2</sub>H<sub>5</sub>), but-2-in-1-yl (-CH<sub>2</sub>-C≡C-CH<sub>3</sub>), but-3-in-1-yl (-CH<sub>2</sub>)<sub>2</sub>-C≡CH) group.

Generally, the term „alkenyl group“ and „alkinyl group“ comprises also compounds having double bonds and, additionally, triple bonds, i.e. „alkeninyl groups“, having preferably one double bond and, additionally, one triple bond. As an example

therefore, the group 4,7-dimethyl-oct-6-en-2-in-1-yl ( $-\text{CH}_2-\text{C}\equiv\text{C}-\text{CH}(\text{CH}_3)-\text{CH}_2-\text{CH}=\text{C}(\text{CH}_3)_2$ ) may be given.

Number of rings: Generally, all the cyclic groups have one, two, three or more rings in the group, preferably one or two rings, more preferably one ring. Two or more rings can be connected by ring annelation, by a single bond or by a spiro atom. This fact also relates, independently of each other, to cycloalkyl, cycloalkenyl, cycloalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, as well as to other cyclic groups.

Generally, the terms „alkyl, alkenyl, and alkynyl“ refer also to groups, in which one, two, three, four, five or more, preferably three, most preferably one of the hydrogen atoms, independently of each other, are substituted by a halogen atom. The term “halogen atom” comprises a fluorine (-F), chlorine (-Cl), bromine (-Br), iodine (-I), respectively. The preferred halogen atoms for substitution are fluorine and chlorine, especially fluorine. Therefore, the terms alkyl, alkenyl and alkynyl groups refer also, for example, to 2,2,2-trichloro-eth-1-yl ( $-\text{CH}_2\text{CCl}_3$ ), trifluoromethyl ( $-\text{CF}_3$ ), 2,2,2-trifluoro-eth-1-yl ( $-\text{CH}_2\text{CF}_3$ ) or pentafluoro-ethyl ( $-\text{CF}_2\text{CF}_3$ ) group. This kind of substitution also relates to cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl groups mentioned below and correspondingly to all other groups mentioned in this application. Further examples therefore are given at the corresponding paragraphs for the definition.

Furthermore, the hydrogen atoms of the alkyl, alkenyl, and alkynyl groups may be further substituted, independently of each other, by hydroxy (-OH), oxo (=O), thiol (-SH), thio (=S), amino (-NH<sub>2</sub>), imino (=NH), oder nitro (-NO<sub>2</sub>). This kind of substitution also relates to cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl groups mentioned below and correspondingly to all other groups mentioned in this application. Examples therefore are given at the corresponding paragraphs for the definition.

Under a „linear alkyl group“ an alkyl group with a single straight carbon chain - without a branching point - is understood, which is derived, for example, from „normal-alkanes“ or „n-alkanes“.

Examples therefore are n-propyl ( $-\text{CH}_2\text{-CH}_2\text{-CH}_3$ ), n-butyl ( $-\text{CH}_2\text{-CH}_2\text{-CH}_2\text{-CH}_3$ ) or n-amyl ( $-\text{CH}_2\text{-CH}_2\text{-CH}_2\text{-CH}_2\text{-CH}_3$ ).

Under a „branched alkyl group“ an alkyl group is understood which has one, two, three or more branching points, preferably one branching point, in the carbon chain of the alkane. Branched alkyl groups are derived, for example, from iso-alkanes or neo-alkanes.

Examples therefore are iso-propyl ( $-\text{CH}(\text{CH}_3)_2$ ), iso-butyl ( $-\text{CH}_2\text{CH}(\text{CH}_3)_2$ ), sec-butyl ( $-\text{CH}(\text{CH}_3)(\text{CH}_2\text{CH}_3)$ ), tert-butyl ( $-\text{C}(\text{CH}_3)_3$ ), or neo-amyl ( $-\text{CH}_2\text{C}(\text{CH}_3)_3$ ); the branching point is marked in bold type.

These definitions shall be deemed to be valid for all other groups mentioned correspondingly.

The term „cycloalkyl“ refers to a saturated, substituted or unsubstituted, cyclic hydrocarbon group having 3 to 30 carbon atoms, preferably 3 to 20 carbon atoms, more preferably 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 carbon atoms. Preferably, the cycloalkyl group contains 3, 4, 5, 6, 7, 8, 9 or 10 carbon atoms in the ring.

Concrete examples for a substituted or unsubstituted cycloalkyl group comprise cyclopropyl, cyclobutyl, cyclopentyl, 2-methyl-cyclopent-1-yl, 3-methyl-cyclopent-1-yl, cyclohexyl, 2-methyl-cyclohex-1-yl, 3-methyl-cyclohex-1-yl, 4-methyl-cyclohex-1-yl, 4-ethyl-cyclohex-1-yl; 4-isopropyl-cyclohex-1-yl, 3,5-dimethyl-cyclohex-1-yl, cycloheptyl, cyclooctyl; 4-isopropyl-cyclooct-1-yl, (4-cyclopentyl)-cyclohexyl, spiro[4,5]-decanyl, norbornyl, decalanyl, cubanyl, bicyclo[4.3.0.]-nonyl, tetralinyl, or fluoro-cyclohexyl group.

Further examples for a substituted cycloalkyl group are cyclopentan-1-on-2-yl, cyclopentan-1-on-3-yl, cyclohexan-1-on-2-yl, cyclohexan-1-on-3-yl, cyclohexan-1-on-4-yl group.

The term "cycloalkenyl" refers to a partially unsaturated, substituted or unsubstituted, cyclic hydrocarbon group having 3 to 30 carbon atoms, preferably 3 to 20 carbon atoms, more preferably 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 carbon atoms. Preferably, the cycloalkenyl group contains 3, 4, 5, 6, 7, 8, 9 or 10 carbon atoms in the ring. The cycloalkenyl group has one or two or three double bonds, preferably one or two double bonds, more preferably one double bond; the double may be exocyclic or endocyclic, preferably endocyclic.

Concrete examples for a substituted or unsubstituted cycloalkenyl group comprise cyclopent-1-en-1-yl, 2-methyl-cyclopent-1-en-1-yl, 3-methyl-cyclopent-1-en-1-yl, 4-methyl-cyclopent-1-en-1-yl, 5-methyl-cyclopent-1-en-1-yl, cyclopent-1-en-3-yl, cyclopent-1-en-4-yl, cyclopenta-1,3-dien-5-yl, cyclohex-1-en-1-yl, cyclohex-1-en-3-yl, cyclohex-1-en-4-yl, 2-methyl-cyclohex-1-en-1-yl, 3-methyl-cyclohex-1-en-1-yl, 4-methyl-cyclohex-1-en-1-yl, 5-methyl-cyclohex-1-en-1-yl, 6-methyl-cyclohex-1-en-1-yl, 1-methyl-cyclohex-1-en-3-yl, 2-methyl-cyclohex-1-en-3-yl, 3-methyl-cyclohex-1-en-3-yl, 4-methyl-cyclohex-1-en-3-yl, 5-methyl-cyclohex-1-en-3-yl, 6-methyl-cyclohex-1-en-3-yl, cyclohexa-1,3-dien-1-yl, cyclohexa-1,3-dien-2-yl, cyclohexa-1,3-dien-5-yl, 4-methylen-cyclohex-1-yl, or 4-(propyl-2-en)-cyclohex-1-yl group.

Further examples for a cycloalkenyl group are cyclopent-2-en-1-on-2-yl, cyclopent-2-en-1-on-3-yl, cyclohex-2-en-1-on-2-yl, cyclohex-2-en-1-on-3-yl, cyclohex-2-en-1-on-4-yl.

The term "cycloalkinyl" refers to a partially unsaturated, substituted or unsubstituted, cyclic hydrocarbon group having 6 to 30 carbon atoms, preferably 6 to 20 carbon atoms, more preferably 6, 7, 8, 9, 10, 11, or 12 carbon atoms. Preferably, the cycloalkinyl group contains 6, 7, 8, 9 or 10 carbon atoms in the ring. The cycloalkinyl group has one or two triple bonds, preferably one triple bond. The triple bond may be exocyclic or endocyclic, preferably endocyclic.

Concrete examples are the cyclooct-1-in-3-yl, cyclooct-1-in-4-yl and the cyclooct-1-in-5-yl group.

The terms "heteroalkyl" refers to a saturated, linear or branched, substituted or unsubstituted hydrocarbon group having 1 to 30 carbon atoms, preferably 1 to 20

carbon atoms, more preferably 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 carbon atoms, wherein one or more carbon atoms, independently of each other, are substituted by nitrogen, oxygen, or sulfur. Generally, one, two or three carbon atoms are substituted by nitrogen, oxygen, or sulfur, preferably one or two, more preferably one.

Furthermore, the term "heteroalkyl" also refers to a carboxylic acid group or a group derived from a carboxylic acid group, as for example acyl, acyl-alkyl, alkoxycarbonyl, acyloxy, acyloxyalkyl, carboxyalkylamid, alkoxycarbonyloxy. Further examples for heteroalkyl groups are nitrile, isonitrile, cyanat, isocyanat, thiocyanat, isothiocyanat, carbonyl in combination with alkyl groups.

Concrete examples for an "heteroalkyl" group comprise

methoxy ( $-\text{OCH}_3$ ), hydroxymethyl ( $-\text{CH}_2\text{-OH}$ ), carboxy-methyl ( $-\text{CH}_2\text{-COOH}$ ), carboxamide-methyl ( $-\text{CH}_2\text{-CO-NH}_2$ ), trifluoromethoxy ( $-\text{OCF}_3$ ), ethoxy ( $-\text{OC}_2\text{H}_5$ ), hydroxy-ethyl ( $-\text{CH}_2\text{-CH}_2\text{-OH}$ ), hydroxy-ethoxyl ( $-\text{O-CH}_2\text{-CH}_2\text{-OH}$ ), amino-ethoxyl ( $-\text{O-CH}_2\text{-CH}_2\text{-NH}_2$ ), di-N,N-(hydroxy-ethyl)-amino ( $-\text{N}(\text{CH}_2\text{-CH}_2\text{-OH})_2$ ), n-propoxy ( $-\text{O-n-C}_3\text{H}_7$ ), iso-propoxy ( $-\text{O-CH}(\text{CH}_3)_2$ ), 2-hydroxy-prop-1-yl ( $-\text{CH}_2\text{-CH}(\text{OH})\text{-CH}_3$ ), n-butoxy ( $-\text{O-n-C}_4\text{H}_{10}$ ), tert-butoxy ( $-\text{OC}(\text{CH}_3)_3$ ), methoxy-methyl ( $-\text{CH}_2\text{-O-CH}_3$ ), ethoxy-methyl ( $-\text{CH}_2\text{-O-C}_2\text{H}_5$ ), 2-methoxy-ethyl ( $-(\text{CH}_2)_2\text{-O-CH}_3$ ), 2-ethoxy-ethyl ( $-(\text{CH}_2)_2\text{-O-C}_2\text{H}_5$ ), 2'-hydroxy-2-ethoxy-ethyl ( $-(\text{CH}_2)_2\text{-O-}(\text{CH}_2)_2\text{-OH}$ ), 2'-hydroxy-2-ethoxy-ethoxy ( $-\text{O-}(\text{CH}_2)_2\text{-O-}(\text{CH}_2)_2\text{-OH}$ ), enol ethers; or

N-methyl-amino ( $-\text{NH}(\text{CH}_3)$ ), N,N-dimethylamino ( $-\text{N}(\text{CH}_3)_2$ ), N-ethyl-amino ( $-\text{NH}(\text{C}_2\text{H}_5)$ ), N,N-diethyl-amino ( $-\text{N}(\text{C}_2\text{H}_5)_2$ ), N-isopropyl-amino ( $-\text{NH}(\text{CH}(\text{CH}_3)_2)$ ), N-ethyl-N-isopropyl-amino ( $-\text{N}(\text{C}_2\text{H}_5)(\text{CH}(\text{CH}_3)_2)$ ), N,N-diisopropyl-amino ( $-\text{N}(\text{CH}(\text{CH}_3)_2)_2$ ), N-methyl-amino-methyl ( $-\text{CH}_2\text{-NH}(\text{CH}_3)$ ), N-ethyl-amino-methyl ( $-\text{CH}_2\text{-NH}(\text{C}_2\text{H}_5)$ ), N,N-dimethylamino-methyl ( $-\text{CH}_2\text{-N}(\text{CH}_3)_2$ ), N,N-diisopropyl-amino-ethyl ( $-(\text{CH}_2)_2\text{-N}(\text{CH}(\text{CH}_3)_2)_2$ ), 2-(N,N-dimethyl-amino)-ethyl ( $-(\text{CH}_2)_2\text{-N}(\text{CH}_3)_2$ ), 2-(N,N-diethyl-amino)-ethoxy ( $-\text{O-}(\text{CH}_2)_2\text{-N}(\text{C}_2\text{H}_5)_2$ ); or

methyl-mercapto ( $-\text{SCH}_3$ ), ethyl-mercapto ( $-\text{SC}_2\text{H}_5$ ), n-propyl-mercapto ( $-\text{S-n-C}_3\text{H}_7$ ), n-butyl-mercapto ( $-\text{S-n-C}_4\text{H}_{10}$ ) group; or

acetyl ( $-\text{CO-CH}_3$ ), propionyl ( $-\text{CO-C}_2\text{H}_5$ ), butyryl ( $-\text{CO-n-C}_3\text{H}_7$ ), acetyloxy ( $-\text{O-CO-CH}_3$ ), propionyloxy ( $-\text{O-CO-C}_2\text{H}_5$ ), butyryloxy ( $-\text{O-CO-C}_3\text{H}_7$ ), methoxy-carbonyl ( $-\text{CO-CH}_3$ ),

OCH<sub>3</sub>), ethoxy-carbonyl (-CO-OC<sub>2</sub>H<sub>5</sub>), 2'-hydroxy-ethoxy-carbonyl (-CO-O-(CH<sub>2</sub>)<sub>2</sub>-OH), methoxy-carbonyloxy (-O-CO-OCH<sub>3</sub>), ethoxy-carbonyloxy (-O-CO-OC<sub>2</sub>H<sub>5</sub>), dimethylamino-carbonyl (-CO-N(CH<sub>3</sub>)<sub>2</sub>), N-methyl-N-ethyl-amino-carbonyl (-CO-N(CH<sub>3</sub>)(C<sub>2</sub>H<sub>5</sub>)), di-N,N-(2'-hydroxy-ethyl) amino-carbonyl (-CO-N(CH<sub>2</sub>-CH<sub>2</sub>-OH)<sub>2</sub>), N-methyl-N-ethyl-amino-carbonyloxy (-O-CO-N(CH<sub>3</sub>)(C<sub>2</sub>H<sub>5</sub>)), dimethylamino-carbonyloxy (-O-CO-N(CH<sub>3</sub>)<sub>2</sub>), ureyl (-NH-CO-NH<sub>2</sub>), N,N-dimethyl-ureyl (-NH-CO-N(CH<sub>3</sub>)<sub>2</sub>) group; or

nitrile (-C≡N), nitrilo-methyl (-CH<sub>2</sub>-C≡N), 2-nitrilo-ethyl (-(CH<sub>2</sub>)<sub>2</sub>-C≡N), isonitrile (-N=C), isonitrilo-methyl (-CH<sub>2</sub>-N=C), cyanat (-O-C≡N), isocyanat (-N=C=O), thiocyanat (-S-C≡N), isothiocyanat (-N=C=S), formyl (-CHO), formyl-methyl (-CH<sub>2</sub>-CHO), 2-formyl-ethyl (-(CH<sub>2</sub>)<sub>2</sub>-CHO) group.

The terms "heteroalkenyl" refers to an unsaturated, linear or branched, substituted or unsubstituted hydrocarbon group having 2 to 30 carbons atoms, preferably 2 to 20 carbon atoms, more preferably 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 carbon atoms, wherein one or more carbon atoms, independently of each other, are substituted by nitrogen, oxygen, or sulfur. Generally, one, two or three carbon atoms are substituted by nitrogen, oxygen, or sulfur, preferably one or two, more preferably one. The heteroalkenyl group has one or two or three double bonds, preferably one or two double bond, more preferably one double bond. Concrete examples for an heteroalkenyl group comprise allyloxy (-O-CH<sub>2</sub>CH=CH<sub>2</sub>), 2-methyl-prop-2-enyl-1-oxy (-O-CH<sub>2</sub>C(CH<sub>3</sub>)=CH<sub>2</sub>), allylamino (-NH(CH<sub>2</sub>CH=CH<sub>2</sub>)), N,N-diallylamino (-N(CH<sub>2</sub>CH=CH<sub>2</sub>)<sub>2</sub>) group.

The term "heterocycloalkyl" refers to a saturated, substituted or unsubstituted, cyclic hydrocarbon group having 1 to 30 carbons atoms, preferably 1 to 20 carbon atoms, more preferably 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 carbon atoms. Preferably, the heterocycloalkyl group contains 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 carbon atoms in the ring, wherein one, two, three or more ring carbon atoms, independently of each other, are substituted by nitrogen, oxygen, or sulfur. Generally, one, two or three ring carbon atoms are substituted by nitrogen, oxygen, or sulfur, preferably one or two, more



preferably one. The hetero atoms may be a part of the ring or substituents attached to the ring, preferably they are a part of the ring.

Concrete examples of a heterocycloalkyl group comprise a substituted or unsubstituted oxirano, aziridino, oxacyclopropyl, azacyclopropyl, thiirano, oxetano, thietano, pyrrolidino, tetrahydrofurano, thiolano, 1,1-dioxo-thiolano, 1,3-dioxolano, thiazolidino, imidazolidino, oxazolidino, pyrazolidino, tetrahydropyrano, piperidino, urotropino, piperazino, N-methyl-piperazino, (2-(N-methyl)-N'-piperazinyl)-ethyl, (4N-(2'-hydroxyethyl)-1N-piperazinyl), (2-(4N-(2'-hydroxyethyl)-1N-piperazinyl)-ethyloxy), morpholino, 2-(N-morpholino)-ethyl group, as well as lactames, lactones, cyclic imides and cyclic anhydrides.

The term "heterocycloalkenyl" refers to an unsaturated, substituted or unsubstituted, cyclic hydrocarbon group having 2 to 30 carbons atoms, preferably 2 to 20 carbon atoms, more preferably 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 carbon atoms. Preferably, the heterocycloalkenyl group contains 2, 3, 4, 5, 6, 7, 8, 9 or 10 carbon atoms in the ring, wherein one or more ring carbon atoms, independently of each other, are substituted by nitrogen, oxygen, or sulfur. Generally, one, two or three ring carbon atoms are substituted by nitrogen, oxygen, or sulfur, preferably one or two, more preferably one. The hetero atoms may be a part of the ring or substituents attached to the ring, preferably they are a part of the ring. The heterocycloalkenyl group has one or two or three double bonds, preferably one or two double bonds, more preferably one double bond; the double may be exocyclic or endocyclic, preferably endocyclic.

Concrete examples of a heterocycloalkyl group comprise substituted or unsubstituted pyrrolinyl, 2,3-dihydrofuranyl, 2,5-dihydrofuranyl, 2,3-dihydrothiophenyl, 1,1-dioxo-2,5-dihydro-thiophenyl, 2,5-dihydrothiophenyl, thiazolinyl, imidazolinyl, oxazolinyl, pyrazolinyl group.

The term "aryl" refers to a carbocyclic, aromatic, substituted or unsubstituted hydrocarbon group having 5 to 30 carbons atoms, preferably 5 to 20 carbon atoms, more preferably 5, 6, 7, 8, 9, 10, 11, or 12 carbon atoms. The aryl group has generally one, two, three or more rings, preferably one or two rings, more preferably

one ring, wherein the rings may be connected by annellation or by a single bond. Generally, the aryl group has 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14 ring carbon atoms, preferably 6, 7, 8, 9, or 10 ring carbon atoms, more preferably 6 ring carbon atoms. Concrete examples for a substituted or unsubstituted aryl group comprise substituted or unsubstituted phenyl, 4-fluoro-phenyl, 3-fluoro-phenyl, pentafluoro-phenyl, 4-hydroxyphenyl, 3-nitro-phenyl, 4-(trifluoromethyl)-phenyl, 4-anilinyl, 2-biphenyl, 3-biphenyl, 4-biphenyl, indenyl, 1-naphthyl, or 2-naphthyl, 1-anthracenyl, 2-anthracenyl, 3-anthracenyl, group.

The term "heteroaryl" refers to a aromatic, substituted or unsubstituted hydrocarbon group having 1 to 30 carbons atoms, preferably 1 to 20 carbon atoms, more preferably 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 carbon atoms, and, furthermore, the heteroaryl group has 1, 2, 3, 4, 5, or 6 hetero atoms, preferably 1, 2, 3, or 4, more preferably 1, 2 or 3 hetero atoms, further more preferably 1 or 2 hetero atoms and, most preferably 1 hetero atom, which are independently of each other selected from oxygen, nitrogen and sulfur. The hetero atoms may be a part of the ring or a part of the substituent, preferably, they are a part of the ring. The aryl group has generally one, two, three or more rings, preferably one or two rings, more preferably one ring, wherein the rings may be connected by annellation or by a single bond. Generally, the heteroaryl group has 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14 ring carbon atoms, preferably 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 ring carbon atoms, as well as 1, 2, 3, 4, or 5 ring heteroatoms, preferably 1, 2, or 3 ring heteroatoms, further more preferably 1 or 2 ring heteroatoms, most preferably 1 ring heteroatom.

Concrete examples for a substituted or unsubstituted heteroaryl group comprise substituted or unsubstituted furanyl, thiophenyl, pyrrolyl, oxazolyl, thiazolyl, 1-imidazolyl, 2-imidazolyl, 4-imidazolyl, 3-phenyl-1-pyrrolyl, isoxazolyl, isothiazolyl, 3-pyrazolyl, 1,2,3-triazolyl, 1,2,4- triazolyl, tetrazolyl, 4-pyridinyl, 3-pyridinyl, 2-pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, indazolyl, 6-indolyl, benzimidazolyl, chinolynyl, isochinolynyl, purinyl, carbazolinyl, acridinyl, and 2,3'-bifuryl group.

The term "aryl-alkyl" refers to an aryl group as defined above and an alkyl group as defined above. Therefore, an aryl-alkyl group has at least one, two or more

substituted or unsubstituted aryl groups, preferable one or two aryl groups, more preferably one aryl group, as defined above, and further, one, two or more substituted or unsubstituted alkyl groups, preferable one or two alkyl groups, more preferably one alkyl group, as defined above.

Concrete examples for a substituted or unsubstituted aryl-alkyl group comprise substituted or unsubstituted benzyl, 2-phenyleth-1-yl, p-tolyl-methyl, p-tolyl-ethyl, 2-(4-ethyl-phenyl)-eth-1-yl group p-tolyl, m-tolyl, o-tolyl, 2,3-dimethyl-phenyl, 2,4-dimethyl-phenyl, 2,5-dimethyl-phenyl, 2,6-dimethyl-phenyl, 3,4-dimethyl-phenyl, 3,5-dimethyl-phenyl, 2,4,6-trimethyl-phenyl, benzhydryl (= diphenyl-methyl), trityl (= triphenyl-methyl),  $\alpha$ -styryl,  $\beta$ -styryl, cumyl, 2-ethyl-phenyl, 3-ethyl-phenyl, 4-ethyl-phenyl, 2-fluoro-benzyl, 1-methyl-2-fluoro-phen-6-yl, 1-methyl-2-fluoro-phen-4-yl, 1H-indenyl, indanyl, indan-1-on-2-yl, tetralinyl, fluorenyl, (3-phenyl)-cyclopent-1-yl, dihydronaphthalinyl, or (4-cyclohexyl)-phenyl, group.

The term "heteroaryl-alkyl" refers to an heteroaryl group as defined above, and an alkyl group as defined above. Therefore, an aryl-alkyl group has at least one, two or more substituted or unsubstituted heteroaryl groups, preferably one or two heteroaryl groups, more preferably one heteroaryl group, as defined above, and further, one, two or more substituted or unsubstituted alkyl groups, preferable one or two alkyl groups, more preferably one alkyl group, as defined above.

Concrete examples for a substituted or unsubstituted heteroaryl-alkyl group comprise substituted or unsubstituted N-methyl-pyrrol-2-yl, N-methyl-pyrrol-3-yl, 2-methyl-pyrrol-1-yl, (2-methyl-pyrrol-1-yl)-methyl, 3-methyl-pyrrol-1-yl, 4-pyridino-methyl, 4-pyridino-ethyl, 2-(thiazol-2-yl)-ethyl, tetrahydroisochinolyl, 2-ethyl-indol-1-yl, 3-ethyl-indol-1-yl, 4-methyl-pyridin-2-yl, 4-methyl-pyridin-3-yl, group.

The term "aryl-heteroalkyl" refers to an aryl group as defined above and a heteroalkyl group as defined above. Therefore, an aryl-heteroalkyl group has at least one, two or more substituted or unsubstituted aryl groups, preferable one or two aryl groups, more preferably one aryl group, as defined above, and further, one, two or more substituted or unsubstituted heteroalkyl groups, preferable one or two heteroalkyl groups, more preferably one heteroalkyl group, as defined above.

Concrete examples for a substituted or unsubstituted aryl-heteroalkyl group comprise phenoxy, phenylamino, diphenylamino, benzyloxy, dibenzylamino, 2-methoxy-phenyl, 3-methoxy-phenyl, 4-methoxy-phenyl, 4-ethoxy-phenyl, 2-phenylethyloxy, 2-phenylethylamino or (2-(4-dimethylamino)-phenyl)-eth-1-oxy, (4-carboxyphenyl) alkyl group, benzoyl ( $-\text{CO}-\text{C}_6\text{H}_5$ ), phenylacetyl ( $-\text{CO}-\text{CH}_2-\text{C}_6\text{H}_5$ ), phenacyl ( $-\text{CH}_2-\text{CO}-\text{C}_6\text{H}_5$ ) group.

The term "heteroaryl-heteroalkyl" refers to a heteroaryl group as defined above and a heteroalkyl group as defined above. Therefore, a heteroaryl-heteroalkyl group has at least one, two or more substituted or unsubstituted heteroaryl groups, preferably one or two heteroaryl groups, more preferably one heteroaryl group, as defined above, and further, one, two or more substituted or unsubstituted heteroalkyl groups, preferably one or two heteroalkyl groups, more preferably one heteroalkyl group, as defined above.

Concrete examples for a substituted or unsubstituted heteroaryl-heteroalkyl group comprise substituted or unsubstituted 2-(4-pyridino-ethyl)-amino, 2-(4-pyridino-methyl)oxy, 2-(2-thiazolo-ethyl)-amino group.

**Combinations:** Also within the scope of the present invention are combinations of two, three or more groups, preferably two groups listed above, which are not mentioned explicitly, for example aryl-heteroaryl, heterocycloalkyl-aryl, cycloalkyl-aryl, heterocycloalkyl-heteroaryl, cycloalkenyl-heteroaryl, heterocycloalkenyl-aryl, etc..

Concrete examples therefore are 4-phenyl-cyclohex-1-yl, 4-phenyl-cyclohex-1-en-1-yl, 4-(2-pyridinyl)-cyclohex-1-yl, 4-(2-pyridinyl)-cyclohex-1-en-1-yl, 4N-phenyl-piperazin-1N-yl, 5-phenyl-1H-tetrazol-1-yl, 4N-(2-(5-phenyl)-thiazolyl)-piperazin-1N-yl group.

The term "halogen" comprises fluorine ( $-\text{F}$ ), chlorine ( $-\text{Cl}$ ), bromine ( $-\text{Br}$ ), and iodine ( $-\text{I}$ ), respectively.

The term „electron withdrawing group“ refers to a atom with a high electronegativity on the Pauling scale or a comparable group capable of withdrawing electrons, like groups having a double or triple bound and having hetero atoms like nitrogen, oxygen and sulfur; The term „electron withdrawing group“ comprises further two single bound atoms or one double bound atom. Examples for an „electron withdrawing group“ are the halogen atoms fluorine (-F), chlorine (-Cl), bromine (-Br), iodine (-I), and the double bound oxygen atom (=O). As an example for the „electron withdrawing group“, the cyano group (-C≡N) may be given. Preferred as an „electron withdrawing group“ are two single bound fluorine atoms (-F)<sub>2</sub> and the double bound oxygen atom (=O), especially preferred is the the double bound oxygen atom (=O).

**Glutamine:** Throughout the description the expression "glutamine" or "glutaminy", respectively, should be considered in that "homoglutamine" or "homoglutaminy", respectively, is also comprised within this wording, i.e., the amino acids mentioned above may have L and D configuration in the Fischer projection, as well as an amino group in  $\alpha$  or  $\beta$  position of the carbon chain. Preferably the wording "glutamine" or "glutaminy" comprises the group L- $\alpha$ -glutamine (-CO-CH(NH<sub>2</sub>)-(CH<sub>2</sub>)<sub>2</sub>-CO-NH<sub>2</sub>), L- $\alpha$ -homoglutamine (-CO-CH(NH<sub>2</sub>)-(CH<sub>2</sub>)<sub>3</sub>-CO-NH<sub>2</sub>), and L- $\beta$ -homoglutamine (-CO-CH<sub>2</sub>-CH(NH<sub>2</sub>)-(CH<sub>2</sub>)<sub>2</sub>-CO-NH<sub>2</sub>), most preferably L- $\alpha$ -glutamine.

**Stereoisomers:**

All possible stereoisomers of the claimed compounds are included in the present invention. Especially preferred for the glutamine group are the L- $\alpha$ -glutamine (-CO-CH(NH<sub>2</sub>)-(CH<sub>2</sub>)<sub>2</sub>-CO-NH<sub>2</sub>), L- $\alpha$ -homoglutamine (-CO-CH(NH<sub>2</sub>)-(CH<sub>2</sub>)<sub>3</sub>-CO-NH<sub>2</sub>), and L- $\beta$ -homoglutamine (-CO-CH<sub>2</sub>-CH(NH<sub>2</sub>)-(CH<sub>2</sub>)<sub>2</sub>-CO-NH<sub>2</sub>) group, most preferred is the L- $\alpha$ -glutamine group.

Concerning the stereoisomers of the prolin mimetica, all possible stereoisomers of the compounds having proline mimetica of the structural formulas (II) to (IX) of the present invention are included in this application. Especially, that configuration at the "α carbon atom" of the prolin-mimetica of the structural formulas (II) to (IX) of the present invention is preferred, which imitates the stereochemical configuration of the

naturally occurring amino acid L- $\alpha$ -proline at its  $\alpha$  carbon atom. Therefore, prolin mimetica of the structural formulas (II) to (IX) of the present invention have preferably that stereochemical configuration at the " $\alpha$  carbon atom", which corresponds to the stereochemical configuration of L- $\alpha$ -proline at its  $\alpha$  carbon atom.

Naturally occurring L- $\alpha$ -proline has an absolute S-configuration at its  $\alpha$ -carbon atom in the sense of the Cahn-Ingold-Prelog nomenclature. If the carboxylic acid group of L- $\alpha$ -proline is imitated by the cyano, 2H-tetrazol-5-yl, or phosphonic acid diphenyl ester group, the preferred configuration will be the S configuration at the  $\alpha$  carbon atom of the prolin mimeticum of the structural formulas (II) to (IX) of the present invention; in the case that the -COOH group of prolin is imitated by a boronic acid group, the absolute configuration at the  $\alpha$  carbon atom of the prolin mimeticum of the structural formulas (II) to (IX) of the present invention will change to R due to the lower molecular mass of a boron atom compared with a carbon atom. Despite the fact that the absolute configuration of the  $\alpha$  carbon atom of the proline mimetica of the structural formulas (II) to (IX) of the present invention may change due to the change of the substituents of the  $\alpha$  carbon atom, the absolute configuration at the  $\alpha$  carbon atom corresponding to that of the naturally occurring amino acid L- $\alpha$ -proline is always preferred.

Where the compounds according to this invention have at least one chiral center, they may accordingly exist as enantiomers. Where the compounds possess two or more chiral centers, they may additionally exist as diastereomers. It is to be understood that all such isomers and mixtures thereof are encompassed within the scope of the present invention. Also comprised within the present invention are all possible stereoisomers of compounds with proline mimetica having stereochemical centers other than that which corresponds to the  $\alpha$  carbon atom of the L- $\alpha$ -proline.

#### Preparation and isolation of stereoisomers:

Where the processes for the preparation of the compounds according to the invention give rise to a mixture of stereoisomers, these isomers may be separated by conventional techniques such as preparative chromatography. The compounds may

be prepared in racemic form, or individual enantiomers may be prepared either by enantiospecific synthesis or by resolution. The compounds may, for example, be resolved into their components enantiomers by standard techniques, such as the formation of diastereomeric pairs by salt formation with an optically active acid, such as (-)-di-p-toluoyl-d-tartaric acid and/or (+)-di-p-toluoyl-l-tartaric acid followed by fractional crystallization and regeneration of the free base. The compounds may also be resolved by formation of diastereomeric esters or amides, followed by chromatographic separation and removal of the chiral auxiliary. Alternatively, the compounds may be resolved using a chiral HPLC column.

**Pharmaceutically acceptable salts:**

In view of the close relationship between the free compounds and the compounds in the form of their salts, whenever a compound is referred to in this context, a corresponding salt is also intended, provided such is possible or appropriate under the circumstances.

The pharmaceutically acceptable salt generally takes a form in which an amino acids basic side chain is protonated with an inorganic or organic acid. Representative organic or inorganic acids include hydrochloric, hydrobromic, perchloric, sulfuric, nitric, phosphoric, acetic, propionic, glycolic, lactic, succinic, maleic, fumaric, malic, tartaric, citric, benzoic, mandelic, methanesulfonic, hydroxyethanesulfonic, benzenesulfonic, oxalic, pamoic, 2-naphthalenesulfonic, p-toluenesulfonic, cyclohexanesulfamic, salicylic, saccharinic or trifluoroacetic acid. All pharmaceutically acceptable acid addition salt forms of the compounds of the present invention are intended to be embraced by the scope of this invention.

**Polymorph crystal forms:**

Furthermore, some of the crystalline forms of the compounds may exist as polymorphs and as such are included in the present invention. In addition, some of the compounds may form solvates with water (i.e. hydrates) or common organic solvents, and such solvates are also encompassed within the scope of this invention. The compounds, including their salts, can also be obtained in the form of their

hydrates, or include other solvents used for their crystallization, which are also encompassed within the scope of this invention.

**Prodrugs:**

The present invention further includes within its scope prodrugs of the compounds of this invention. In general, such prodrugs will be functional derivatives of the compounds which are readily convertible *in vivo* into the desired therapeutically active compound. Thus, in these cases, the methods of treatment of the present invention, the term "administering" shall encompass the treatment of the various disorders described with prodrug versions of one or more of the claimed compounds, but which converts to the above specified compound *in vivo* after administration to the subject. Conventional procedures for the selection and preparation of suitable prodrug derivatives are described, for example, in "Design of Prodrugs", ed. H. Bundgaard, Elsevier, 1985 and the patent applications DE 198 28 113, DE 198 28 114, WO 99/67228 and WO 99/67279 which are fully incorporated herein by reference.

**Protective Groups:**

During any of the processes for preparation of the compounds of the present invention, it may be necessary and/or desirable to protect sensitive or reactive groups on any of the molecules concerned. This may be achieved by means of conventional protecting groups, such as those described in Protective Groups in Organic Chemistry, ed. J.F.W. McOmie, Plenum Press, 1973; and T.W. Greene & P.G.M. Wuts, Protective Groups in Organic Synthesis, John Wiley & Sons, 1991, fully incorporated herein by reference. The protecting groups may be removed at a convenient subsequent stage using methods known from the art.

**Amino acids**

Examples of amino acids which can be used in the present invention are L and D-amino acids, N-methyl-amino acids, aza-amino acids; *allo*- and *threo*-forms of Ile and Thr, which can, e.g. be  $\alpha$ -,  $\beta$ - or  $\omega$ -amino acids, whereof  $\alpha$ -amino acids are preferred.



Examples of amino acids are:

aspartic acid (Asp), glutamic acid (Glu), arginine (Arg), lysine (Lys), histidine (His), glycine (Gly), serine (Ser), cysteine (Cys), threonine (Thr), asparagine (Asn), glutamine (Gln), tyrosine (Tyr), alanine (Ala), proline (Pro), valine (Val), isoleucine (Ile), leucine (Leu), methionine (Met), phenylalanine (Phe), tryptophan (Trp), hydroxyproline (Hyp), beta-alanine (beta-Ala), 2-aminooctanoic acid (Aoa), acetidine-(2)-carboxylic acid (Ace), pipecolic acid (Pip), 3-aminopropionic acid, 4-aminobutyric acid and so forth, alpha-aminoisobutyric acid (Aib), sarcosine (Sar), ornithine (Orn), citrulline (Cit), homoarginine (Har), t-butylalanine (*t*-butyl-Ala), t-butylglycine (*t*-butyl-Gly), N-methylisoleucine (N-Melle), phenylglycine (Phg), cyclohexylalanine (Cha), norleucine (Nle), cysteic acid (Cya) and methionine sulfoxide (MSO), acetyl-Lys, modified amino acids such as phosphoryl-serine (Ser(P)), benzyl-serine (Ser(Bzl)) and phosphoryl-tyrosine (Tyr(P)), 2-aminobutyric acid (Abu), aminoethylcysteine (AECys), carboxymethylcysteine (Cmc), dehydroalanine (Dha), dehydroamino-2-butyric acid (Dhb), carboxyglutaminic acid (Gla), homoserine (Hse), hydroxylysine (Hyl), *cis*-hydroxyproline (*cis*Hyp), *trans*-hydroxyproline (*trans*Hyp), isovaline (Iva), pyroglutamic acid (Pyr), norvaline (Nva), 2-aminobenzoic acid (2-Abz), 3-aminobenzoic acid (3-Abz), 4-aminobenzoic acid (4-Abz), 4-(aminomethyl)benzoic acid (Amb), 4-(aminomethyl)cyclohexanecarboxylic acid (4-Amc), Penicillamine (Pen), 2-amino-4-cyanobutyric acid (Cba), cycloalkane-carboxylic acids. Examples of  $\omega$ -amino acids are e.g.: 5-Ara (aminoraleic acid), 6-Ahx (aminohexanoic acid), 8-Aoc (aminooctanoic acid), 9-Anc (aminovanoic acid), 10-Adc (aminodecanoic acid), 11-Aun (aminoundecanoic acid), 12-Ado (aminododecanoic acid). Further amino acids are: indanylglycine (Igl), indoline-2-carboxylic acid (Idc), octahydroindole-2-carboxylic acid (Oic), diaminopropionic acid (Dpr), diaminobutyric acid (Dbu), naphthylalanine (1-Nal) and (2-Nal), 4-aminophenylalanine (Phe(4-NH<sub>2</sub>)), 4-benzoylphenylalanine (Bpa), diphenylalanine (Dip), 4-bromophenylalanine (Phe(4-Br)), 2-chlorophenylalanine (Phe(2-Cl)), 3-chlorophenylalanine (Phe(3-Cl)), 4-chlorophenylalanine (Phe(4-Cl)), 3,4-chlorophenylalanine (Phe(3,4-Cl<sub>2</sub>)), 3-fluorophenylalanine (Phe(3-F)), 4-fluorophenylalanine (Phe(4-F)), 3,4-fluorophenylalanine (Phe(3,4-F<sub>2</sub>)), pentafluorophenylalanine (Phe(F<sub>5</sub>)), 4-guanidinophenylalanine (Phe(4-guanidino)),

homophenylalanine (hPhe), 3-jodophenylalanine (Phe(3-J)), 4-jodophenylalanine (Phe(4-J)), 4-methylphenylalanine (Phe(4-Me)), 4-nitrophenylalanine (Phe(4-NO<sub>2</sub>)), biphenylalanine (Bip), 4-phosphonomethylphenylalanine (Pmp), cyclohexylglycine (Ghg), 3-pyridinylalanine (3-Pal), 4-pyridinylalanine (4-Pal), 3,4-dehydroproline (A-Pro), 4-ketoproline (Pro(4-keto)), thioproline (Thz), isonipecotic acid (Inp), 1,2,3,4-tetrahydroisoquinolin-3-carboxylic acid (Tic), propargylglycine (Pra), 6-hydroxynorleucine (NU(6-OH)), homotyrosine (hTyr), 3-jodotyrosine (Tyr(3-J)), 3,5-dijodotyrosine (Tyr(3,5-J<sub>2</sub>)), methyltyrosine (Tyr(Me)), 2',6'-dimethyltyrosine (Dmt), 3-NO<sub>2</sub>-tyrosine (Tyr(3-NO<sub>2</sub>)), phosphotyrosine (Tyr(PO<sub>3</sub>H<sub>2</sub>)), alkylglycine, 1-aminoindane-1-carboxylic acid, 2-aminoindane-2-carboxylic acid (Aic), 4-amino-methylpyrrol-2-carboxylic acid (Py), 4-amino-pyrrolidine-2-carboxylic acid (Abpc), 2-aminotetraline-2-carboxylic acid (Atc), diaminoacetic acid (Gly(NH<sub>2</sub>)), diaminobutyric acid (Dab), 1,3-dihydro-2H-isoinole-carboxylic acid (Disc), homocyclohexylalanine (hCha), homophenylalanine (hPhe or Hof), *trans*-3-phenyl-azetidine-2-carboxylic acid, 4-phenyl-pyrrolidine-2-carboxylic acid, 5-phenyl-pyrrolidine-2-carboxylic acid, 3-pyridylalanine (3-Pya), 4-pyridylalanine (4-Pya), styrylalanine, tetrahydroisoquinoline-1-carboxylic acid (Tiq), 1,2,3,4-tetrahydronorharmine-3-carboxylic acid (Tpi),  $\beta$ -(2-thienryl)-alanine (Tha).

"Peptides" are selected from dipeptides to decapeptides, preferred are dipeptides, tripeptides, tetrapeptides and pentapeptides. The amino acids for the formation of the "peptides" can be selected from those listed above.

An "aza-amino acid" is defined as an amino acid where the chiral  $\alpha$ -CH group is replaced by a nitrogen atom, whereas an "aza-peptide" is defined as a peptide, in which the chiral  $\alpha$ -CH group of one or more amino acid residues in the peptide chain is replaced by a nitrogen atom.

Other amino acid substitutions for those encoded in the genetic code can also be included in peptide compounds within the scope of the invention and can be classified within this general scheme. Proteinogenic amino acids are defined as

natural protein-derived  $\alpha$ -amino acids. Non-proteinogenic amino acids are defined as all other amino acids, which are not building blocks of common natural proteins.

"Peptide mimetics" per se are known to a person skilled in the art. They are preferably defined as compounds which have a secondary structure like a peptide and optionally further structural characteristics; their mode of action is largely similar or identical to the mode of action of the native peptide; however, their activity (e.g. as an antagonist or inhibitor) can be modified as compared with the native peptide, especially vis à vis receptors or enzymes. Moreover, they can imitate the effect of the native peptide (agonist). Examples of peptide mimetics are scaffold mimetics, non-peptidic mimetics, peptoides, peptide nucleic acids, oligopyrrolinones, vinylogpeptides and oligocarbamates. For the definitions of these peptide mimetics see Lexikon der Chemie, Spektrum Akademischer Verlag Heidelberg, Berlin, 1999.

The aim for using these mimetic structures is increasing the activity, increasing the selectivity to decrease side effects, protect the compound against enzymatic degradation for prolongation of the effect.

The term "subject" as used herein, refers to an animal, preferably a mammal, most preferably a human, who has been the object of treatment, observation or experiment.

The term "therapeutically effective amount" as used herein, means that amount of active compound or pharmaceutical agent that elicits the biological or medicinal response in a tissue system, animal or human, being sought by a researcher, veterinarian, medical doctor or other clinician, which includes alleviation of the symptoms of the disease or disorder being treated.

As used herein, the term "composition" is intended to encompass a product comprising the claimed compounds in the therapeutically effective amounts, as well as any product which results, directly or indirectly, from combinations of the claimed compounds.

**Carriers and Additives for galenic formulations:**

Thus, for liquid oral preparations, such as for example, suspensions, elixirs and solutions, suitable carriers and additives may advantageously include water, glycols, oils, alcohols, flavoring agents, preservatives, coloring agents and the like; for solid oral preparations such as, for example, powders, capsules, gelcaps and tablets, suitable carriers and additives include starches, sugars, diluents, granulating agents, lubricants, binders, disintegrating agents and the like.

Carriers, which can be added to the mixture, include necessary and inert pharmaceutical excipients, including, but not limited to, suitable binders, suspending agents, lubricants, flavorants, sweeteners, preservatives, coatings, disintegrating agents, dyes and coloring agents.

Soluble polymers as targetable drug carriers can include polyvinylpyrrolidone, pyran copolymer, polyhydroxypropylmethacrylamidephenol, polyhydroxyethylaspartamidephenol, or polyethyleneoxidepolylysine substituted with palmitoyl residue. Furthermore, the compounds of the present invention may be coupled to a class of biodegradable polymers useful in achieving controlled release of a drug, for example, polyactic acid, polyepsilon caprolactone, polyhydroxy butyeric acid, polyorthoesters, polyacetals, polydihydropyrans, polycyanoacrylates and cross-linked or amphipathic block copolymers of hydrogels.

Suitable binders include, without limitation, starch, gelatin, natural sugars such as glucose or betalactose, corn sweeteners, natural and synthetic gums such as acacia, tragacanth or sodium oleate, sodium stearate, magnesium stearate, sodium benzoate, sodium acetate, sodium chloride and the like.

Disintegrators include, without limitation, starch, methyl cellulose, agar, bentonite, xanthan gum and the like.

**Indications:**

The term "indications" comprises the following diseases, respectively, the following diseases in mammals, preferably humans, can be treated by the compounds of the present invention:

**metabolic diseases** like impaired glucose tolerance, glucosuria, hyperlipidemia, metabolic acidosis, diabetes mellitus, non-insulin dependent diabetes mellitus, diabetic neuropathy and nephropathy and of sequelae caused by diabetes mellitus;

**neurodegenerative diseases**; high blood pressure and disturbance of signal action at the cells of the islets of Langerhans and insulin sensitivity in the peripheral tissue in the postprandial phase; the metabolism-related hypertension and cardiovascular sequelae caused by hypertension;

**dermal diseases** like skin diseases and diseases of the mucosae;

**immune and autoimmune disorders**, multiple sclerosis, and inflammatory conditions; arthritis; obesity; allograft transplantation; cancer;

**neuronal disorders as well as psychosomatic, neuropsychiatric and depressive illnesses**, such as anxiety, depression, sleep disorders, chronic fatigue, schizophrenia, epilepsy, nutritional disorders, spasm and chronic pain.

The indications above refer each to both acute and chronic form of the disease.

Further, the following diseases can be treated by the compounds of the present invention:

hyperlipidemia, metabolic acidosis, diabetic neuropathy and nephropathy and of sequelae caused by diabetes mellitus in mammals; metabolism-related hypertension and cardiovascular sequelae caused by hypertension in mammals; for the prophylaxis or treatment of skin diseases and diseases of the mucosae, autoimmune diseases and inflammatory conditions, and for the prophylaxis or treatment of psychosomatic, neuropsychiatric and depressive illness, and neurodegenerative diseases such as anxiety, depression, sleep disorders, chronic fatigue, schizophrenia, epilepsy, nutritional disorders, spasm, and chronic pain, and a simple method for the treatment of those disorders.

Most preferably, the following diseases can be treated by the compounds of the present invention: prediabetes, characterized by IGT, IFG or IGM, diabetes mellitus, preferably non-insulin-dependent diabetes mellitus (type 2 diabetes mellitus) and obesity.

#### Classification of Diabetes

The newly revised classification of diabetes mellitus is summarized in Table 1. Clinical diabetes may be divided into four general subclasses, including (1) type 1 (caused by beta cell destruction and characterized by absolute insulin deficiency) (2) type 2 (characterized by insulin resistance and relative insulin deficiency) (3) other specific types of diabetes (associated with various identifiable clinical conditions or syndromes) and (4) gestational diabetes mellitus. In addition to these clinical categories, two conditions – impaired glucose tolerance and impaired fasting glucose – refer to a metabolic state intermediate between normal glucose homeostasis and overt diabetes. These conditions significantly increase the later risk of diabetes mellitus and may in some instances be part of its natural history. It should be noted that patients with any form of diabetes might require insulin treatment at some point. For this reason the previously used terms insulin-dependent diabetes (for type 1 diabetes mellitus) and non-insulin-dependent diabetes (for type 2) have been eliminated.

**Table 1.      Classification of diabetes**

##### *Clinical diabetes*

1.    Type 1 diabetes, formerly called insulin-dependent diabetes mellitus (IDDM) or "juvenile-onset diabetes"
2.    Type 2 diabetes, formerly called non-insulin-dependent diabetes (NIDDM) or "adult-onset diabetes"
3.    Other specific types

- a) Genetic defects of  $\beta$ -cell function (e.g., maturity-onset diabetes of the young [MODY] types 1 – 3 and point mutations in mitochondrial DNA)
  - b) Genetic defects in insulin action
  - c) Disease of the exocrine pancreas (e.g., pancreatitis, trauma, pancreatectomy, neoplasia, cystic fibrosis, hemochromatosis, fibrocalculous pancreatopathy).
  - d) Endocrinopathies (e.g. acromegaly, Cushing's syndrome, hyperthyroidism, pheochromocytoma, glucagonoma, somatostatinoma, aldosteronoma)
  - e) Drug or chemical induced (e.g., glucocorticosteroids, thiazides, diazoxide, pentamidine, vacor, thyroid hormone, phenytoin [Dilantin],  $\beta$ -agonists, oral contraceptives)
  - f) Infections (e.g., congenital rubella, cytomegalovirus)
  - g) Uncommon forms of immune-mediated diabetes (e.g., "stiff-man", syndrome, anti-insulin receptor antibodies)
  - h) Other genetic syndromes (e.g., Down, Klinefelter's, Turner's syndrome, Huntington's disease, myotonic dystrophy, lipodystrophy, ataxia-telangiectasia)
4. Gestational diabetes mellitus

#### *Risk categories*

1. Impaired fasting glucose
2. Impaired glucose tolerance

#### ***Type 1 Diabetes***

Patients with this disorder have little or no insulin secretory capacity and depend on exogenous insulin to prevent metabolic decompensation (e.g., ketoacidosis) and death.

Commonly but not always, diabetes appears abruptly (i.e., over days and weeks) in previously healthy non-obese children or young adults; in older age groups it may have a more gradual onset. At the time of initial evaluation the typical patient often appears ill, has marked symptoms (e.g., polyuria, polydipsia, polyhagia, and weight loss), and may demonstrate ketoacidosis. Type 1 diabetes is believed to have a long asymptomatic preclinical stage often lasting years, during which pancreatic beta cells are gradually destroyed by an autoimmune attack that is influenced by HLA and other genetic factors, as well as the environment. Initially, insulin therapy is essential to restore metabolism toward normal. However, a so-called honeymoon period may follow and last weeks or months, during which time smaller doses of insulin are required because of partial recovery of beta cell function and reversal of insulin resistance caused by acute illness. Thereafter, insulin secretory capacity is gradually lost (over several years). The association of type 1 diabetes with specific immune response (HLA) genes and the presence of antibodies to islet cells and their constituents provides strong support for the theory that type 1 diabetes is an autoimmune disease. This syndrome accounts for less than 10% of diabetes in United States.

### ***Type 2 Diabetes***

Type 2, by far the most common form of the disease, is found in over 90 % of the diabetic patient population. These patients retain a significant level of endogenous insulin secretory capacity. However, insulin levels are low relative to the magnitude of insulin resistance and ambient glucose levels. Type 2 patients are not dependent on insulin for immediate survival and ketosis rarely develops, except under conditions of great physical stress. Nevertheless, these patients may require insulin therapy to control hyperglycemia. Type 2 diabetes typically appears after the age of 40 years, has a high rate of genetic penetrance unrelated to HLA genes, and is associated with obesity. The clinical features of type 2 diabetes may be mild (fatigue, weakness, dizziness, blurred vision, or other non-specific complaints may dominate the picture) or may be tolerated for many years before the patient seeks medical attention.



Moreover, if the level of hyperglycemia is insufficient to produce symptoms, the disease may become evident only after complications develop.

#### ***Other specific types of Diabetes***

This category encompasses a variety of diabetic syndromes attributed to a specific disease, drug, or condition. Genetic research has provided new insights into pathogenesis of MODY, which was formerly included as a form of type 2 diabetes. MODY encompasses several genetic defects of beta cell function, among which mutations at several genetic loci on different chromosomes have been identified. The most common forms – MODY type 3 – is associated with a mutation for a transcription factor encoded on chromosome 12 named hepatocyte nuclear 1 $\alpha$  (HNF 1, also known as TCF1) and –MODY type 2 is associated with mutations of the glucokinase gene (on chromosome 7) Mutations of the HNF-4 $\alpha$  gene (on chromosome 20) are responsible for type 1 of MODY. Each of these conditions is inherited in an autosomal dominant pattern. Two new rare forms of MODY are associated with mutations of the HNF-1 $\beta$  (on chromosome 17) and an insulin gene transcription factor termed PDX-1 or 1DX-1 (on chromosome 13).

The distinction between the various subclasses of diabetes mellitus is usually made on clinical grounds. However, a small subgroup of patients are difficult to classify, that is, they display features common to both type 1 and 2 diabetes. Such patients are commonly non-obese and have reduced insulin secretory capacity that is not sufficient to make them ketosis prone. Many initially respond to oral agents but, with time, require insulin. Some appear to have a slowly evolving form of type 1 diabetes, whereas others defy easy categorization.

#### ***Gestational Diabetes***

The term gestational diabetes describes women with impaired glucose tolerance that appears or is first detected during pregnancy. Gestational diabetes usually

appears in the 2<sup>nd</sup> or 3<sup>rd</sup> trimester, a time when pregnancy-associated insulin antagonistic hormones peak. After delivery, glucose tolerance generally (but not always) reverts to normal.

### ***Diagnosis***

The diagnosis of diabetes is usually straightforward when the classic symptoms of polyuria, polydipsia, and weight loss are present. All that is required is a random plasma glucose measurement from venous blood that is 200 mg/dL or greater. If diabetes is suspected but not confirmed by a random glucose determination, the screening test of choice is overnight fasting plasma glucose level. The diagnosis is established if fasting is equal to or greater than 126 mg/dL on at least two separate occasions.

### ***Related conditions***

#### ***Impaired Glucose Tolerance and Impaired Fasting Glucose***

Impaired glucose tolerance (IGT) and impaired fasting glucose (IFG) are terms applied to individuals who have glucose levels that are higher than normal, (under fed or fasting conditions, respectively) but lower than those accepted as diagnostic for diabetes mellitus. Both conditions are associated with an increased risk for cardiovascular disease, but do not produce the classic symptoms or the microvascular and neuropathic complications associated with diabetes mellitus. In a subgroup of patients (about 25 to 30 %), however, type 2 diabetes eventually develops.

### ***Impaired Glucose Metabolism***

Impaired Glucose Metabolism (IGM) is defined by blood glucose levels that are above the normal range but are high enough to meet the diagnostic criteria for type 2 diabetes mellitus. The incidence of IGM varies from country to country, but usually occurs 2-3 time more frequently than overt diabetes. Until recently, individuals with IGM were felt to be pre-diabetics, but data from several epidemiological studies argue that subjects with IGM are heterogeneous with respect to their risk of diabetes and their risk of cardiovascular morbidity and mortality. The data suggest that subjects with IGM, in particular, those with impaired glucose tolerance (IGT), do not always develop diabetes, but whether they are diabetic or not, they are, nonetheless, at high risk for cardiovascular morbidity and mortality. Among subjects with IGM, about 58 % have Impaired Glucose tolerance (IGT), another 29 % have impaired fasting glucose (IFG), and 13 % have both abnormalities (IFG/IGT). As discussed above, IGT is characterized by elevated post-prandial (post-meal) hyperglycemia while IFG has been defined by the ADA (American Diabetes Association) on the basis of fasting glycemic values.

The categories of (a) normal glucose tolerance (NGT), (b) impaired glucose metabolism (IGM) and (c) overt type 2 diabetes mellitus are periodically revised and adopted by the Expert Committee of the American Diabetes Association (ADA). The actual values as defined in "Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Diabetes Care (26) 1, 2003, 5-20" and "The Diabetes Ready-Reference Guide for Health Care Professionals, 2000, published by the American Diabetes Association" are:

- a) *Normal Glucose Tolerance (NGT)* = fasting glucose level < 6.1 mmol/L or less than 110 mg/dl and a 2h post-prandial glucose level of < 7.8 mmol/L or < 140 mg/dl.
- b) *Impaired Glucose Metabolism (IGM)* is impaired fasting glucose (IFG) defined as IFG = fasting glucose level of 6.1 – 7.0 mmol/L or 110 – 126 mg/dl and/or impaired glucose tolerance (IGT) = a 2h post-

prandial glucose level (75 g OGTT) of 7.8 – 11.1 mmol/L or 140 – 200 mg/dl).

- c) *Type 2 diabetes* = fasting glucose of greater than 7 mmol/L or 126 mg/dl or a 2h post-prandial glucose level (75 g OGTT) of greater than 11.1 mmol/L or 200 mg/dl.

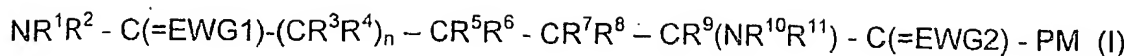
These criteria were defined using the WHO recommended conditions for administration of an oral glucose tolerance test (75 g OGTT) i. e., the oral administration of a glucose load containing the equivalent of 75 g of anhydrous glucose dissolved in water with a blood sample taken 2 hours later to analyze to post-prandial glucose. Other OGTT test conditions have confirmed the associated risks of the IGT and IFG categories including: 1) using 50 g glucose instead of 75 g, 2) using a casual (non-fasting) glucose sample as the analyte, and 3) analysing the post-prandial glucose at 1 hour rather than 2 hours post-glucose load. Under all of these conditions, the glycemic categories defined above have been linked to the increased risks described below, but the standardized OGTT is preferred in order to minimize variations in test results.

Insulin resistance is not primarily due to a diminished number of insulin receptors but to a post-insulin receptor binding defect that is not yet understood. This resistance to insulin responsiveness results in insufficient insulin activation of glucose uptake; oxidation and storage in muscle and inadequate insulin repression of lipolysis in adipose tissue and of glucose production and secretion in the liver.

Accordingly, the compounds and combinations of the present invention are especially useful for the treatment of pathological states, selected from the group consisting of IGT, IFG and IGM.

### **Summary of the invention**

The present invention provides a compound of the formula



wherein  $n$  is 0 or 1;

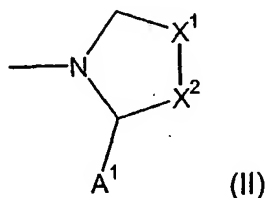
wherein  $\text{R}^1, \text{R}^2, \text{R}^3, \text{R}^4, \text{R}^5, \text{R}^6, \text{R}^7, \text{R}^8, \text{R}^9, \text{R}^{10}$ , and  $\text{R}^{11}$ , independently of each other, are

- a **hydrogen atom** (-H), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group or, a **carbaldehyde** (-CHO), a **ketone** group (-CO-R<sup>20</sup>), a **boronic acid** group (-B(OH)<sub>2</sub>), a **cyano** group (-C≡N), a **carboxylic acid** group (-COOH), a **carboxylic acid ester** group (-COOR<sup>21</sup>), a **carboxylic acid anhydride** group (-CO-O-CO-R<sup>22</sup>), a **hydroxamic acid** group (-CO-NH(OH)), a **N-substituted hydroxamic acid** group (-CO-NR<sup>23</sup>(OH)), a **O-substituted hydroxamic acid** group (-CO-NH(OR<sup>24</sup>)), a **carboxamide** group (-CO-NH<sub>2</sub>), a **N-substituted or N,N-disubstituted carboxylic acid amide** group, (-CO-NHR<sup>25</sup>; -CO-NR<sup>26</sup>R<sup>27</sup>), an **amido** group (-HN-CO-R<sup>28</sup>), a **sulfonic acid** group (-SO<sub>3</sub>H), a **sulfonamide** group (-SO<sub>2</sub>-NH<sub>2</sub>), a **N-substituted or N,N-disubstituted sulfonamide** group (-SO<sub>2</sub>-NHR<sup>29</sup>; -SO<sub>2</sub>-NR<sup>30</sup>R<sup>31</sup>), an **amidosulfone** group (-NH-SO<sub>2</sub>-R<sup>32</sup>), a **sulfone** group (-SO<sub>2</sub>-R<sup>33</sup>), a **phosphoric acid** group (-OP(=O)(OH)<sub>2</sub>), a **phosphoric acid ester** group (-OP(=O)(OR<sup>34</sup>)(OR<sup>35</sup>)), a **phosphonic acid** group (-P(=O)(OH)<sub>2</sub>), an **phosphonic acid ester** group (-P(=O)(OR<sup>36</sup>)(OR<sup>37</sup>)), a **halogen atom**, a **trifluormethyl** group (-CF<sub>3</sub>), a **thiol** group (-SH); a **thioether** group (-S-R<sup>38</sup>), a **hydroxy** group (-OH); an **alkoxy** group (-O-R<sup>39</sup>), a **tetrazole** group, an **amino** group (-NH<sub>2</sub>), or a **N-substituted or N,N-disubstituted amino** group (-NHR<sup>40</sup>; -NR<sup>41</sup>R<sup>42</sup>);
- which each independently can be **substituted** with one or more substituents, which can be the same or different; and,

- wherein optionally, any **two of the groups**  $R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}$ , and  $R^{11}$ , as well the pairs  $R^{26}/R^{27}, R^{30}/R^{31}, R^{34}/R^{35}, R^{36}/R^{37}$  and  $R^{41}/R^{42}$ , independently of each other, may form a part of a ring; and
- wherein the substituents  $R^{20}, R^{21}, R^{22}, R^{23}, R^{24}, R^{25}, R^{26}, R^{27}, R^{28}, R^{29}, R^{30}, R^{31}, R^{32}, R^{33}, R^{34}, R^{35}, R^{36}, R^{37}, R^{38}, R^{39}, R^{40}, R^{41}$ , and  $R^{42}$  independently of each other are a hydrogen atom (-H), or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group; and
- wherein EWG1 and EWG2 are each independently an electron withdrawing group and;

wherein the group PM

has the formula (II)



- wherein  $X^1$  is  $CR^{51}R^{52}$ , O, S, SO, SO<sub>2</sub> or  $NR^{53}$ ; and
- wherein  $X^2$  is  $CR^{54}R^{55}$ , O, S, SO, SO<sub>2</sub>, or  $NR^{56}$ ; and

wherein  $R^{51}, R^{52}, R^{53}, R^{54}, R^{55}$ , and  $R^{56}$ , independently of each other, are

- a hydrogen atom (-H); or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-

heteroalkyl, heteroaryl-heteroalkyl group or, a carbaldehyde (-CHO), a ketone group (-CO-R<sup>60</sup>), a boronic acid group (-B(OH)<sub>2</sub>), a cyano group (-C≡N), a carboxylic acid group (-COOH), a carboxylic acid ester group (-COOR<sup>61</sup>), a carboxylic acid anhydride group (-CO-O-CO-R<sup>62</sup>), a hydroxamic acid group (-CO-NH(OH)), a N-substituted hydroxamic acid group (-CO-NR<sup>63</sup>(OH)), a O-substituted hydroxamic acid group (-CO-NH(OR<sup>64</sup>)), a carboxamide group (-CO-NH<sub>2</sub>), a N-substituted or N,N-disubstituted carboxylic acid amide group, (-CO-NHR<sup>65</sup>; -CO-NR<sup>66</sup>R<sup>67</sup>), an amido group (-HN-CO-R<sup>68</sup>), a sulfonic acid group (-SO<sub>3</sub>H), a sulfonamide group (-SO<sub>2</sub>-NH<sub>2</sub>), a N-substituted or N,N-disubstituted sulfonamide group (-SO<sub>2</sub>-NHR<sup>69</sup>; -SO<sub>2</sub>-NR<sup>70</sup>R<sup>71</sup>), an amidosulfone group (-NH-SO<sub>2</sub>-R<sup>72</sup>), a sulfone group (-SO<sub>2</sub>-R<sup>73</sup>), a phosphoric acid group (-OP(=O)(OH)<sub>2</sub>), a phosphoric acid ester group (-OP(=O)(OR<sup>74</sup>)(OR<sup>75</sup>)), a phosphonic acid group (-P(=O)(OH)<sub>2</sub>), an phosphonic acid ester group (-P(=O)(OR<sup>76</sup>)(OR<sup>77</sup>)), a halogen atom, a trifluormethyl group (-CF<sub>3</sub>), a thiol group (-SH); a thioether group (-S-R<sup>78</sup>), a hydroxy group (-OH); an alkoxy group (-O-R<sup>79</sup>), a tetrazole group, an amino group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted amino group (-NHR<sup>80</sup>; -NR<sup>81</sup>R<sup>82</sup>); and

- which, independently of each other, can be substituted with one or more substituents, which can be the same or different; and,
- wherein optionally, any two of the groups R<sup>51</sup>, R<sup>52</sup>, R<sup>53</sup>, R<sup>54</sup>, R<sup>55</sup>, and R<sup>56</sup>, if present, as well as the pairs R<sup>66</sup>/R<sup>67</sup>, R<sup>70</sup>/R<sup>71</sup>, R<sup>74</sup>/R<sup>75</sup>, R<sup>76</sup>/R<sup>77</sup> and R<sup>81</sup>/R<sup>82</sup>, independently of each other, may form a part of a ring; and
- wherein the substituents R<sup>60</sup>, R<sup>61</sup>, R<sup>62</sup>, R<sup>63</sup>, R<sup>64</sup>, R<sup>65</sup>, R<sup>66</sup>, R<sup>67</sup>, R<sup>68</sup>, R<sup>69</sup>, R<sup>70</sup>, R<sup>71</sup>, R<sup>72</sup>, R<sup>73</sup>, R<sup>74</sup>, R<sup>75</sup>, R<sup>76</sup>, R<sup>77</sup>, R<sup>78</sup>, R<sup>79</sup>, R<sup>80</sup>, R<sup>81</sup>, and R<sup>82</sup>, independently of each other are a hydrogen atom (-H), or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group; and

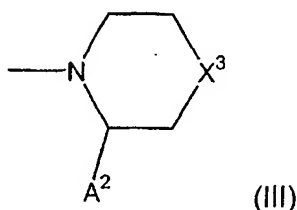
wherein  $A^1$  is

- a hydrogen atom (-H); or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group or, a carbaldehyde (-CHO), a ketone group (-CO-R<sup>100</sup>), a boronic acid group (-B(OH)<sub>2</sub>), a cyano group (-C≡N), a carboxylic acid group (-COOH), a carboxylic acid ester group (-COOR<sup>101</sup>), a carboxylic acid anhydride group (-CO-O-CO-R<sup>102</sup>), a hydroxamic acid group (-CO-NH(OH)), a N-substituted hydroxamic acid group (-CO-NR<sup>103</sup>(OH)), a O-substituted hydroxamic acid group (-CO-NH(OR<sup>104</sup>)), a carboxamide group (-CO-NH<sub>2</sub>), a N-substituted or N,N-disubstituted carboxylic acid amide group, (-CO-NHR<sup>105</sup>; -CO-NR<sup>106</sup>R<sup>107</sup>), an amido group (-HN-CO-R<sup>108</sup>), a sulfonic acid group (-SO<sub>3</sub>H), a sulfonamide group (-SO<sub>2</sub>-NH<sub>2</sub>), a N-substituted or N,N-disubstituted sulfonamide group (-SO<sub>2</sub>-NHR<sup>109</sup>; -SO<sub>2</sub>-NR<sup>110</sup>R<sup>111</sup>), an amidosulfone group (-NH-SO<sub>2</sub>-R<sup>112</sup>), a sulfone group (-SO<sub>2</sub>-R<sup>113</sup>), a phosphoric acid group (-OP(=O)(OH)<sub>2</sub>), a phosphoric acid ester group (-OP(=O)(OR<sup>114</sup>)(OR<sup>115</sup>)), a phosphonic acid group (-P(=O)(OH)<sub>2</sub>), an phosphonic acid ester group (-P(=O)(OR<sup>116</sup>)(OR<sup>117</sup>)), a halogen atom, a trifluormethyl group (-CF<sub>3</sub>), a thiol group (-SH); a thioether group (-S-R<sup>118</sup>), a hydroxy group (-OH); an alkoxy group (-O-R<sup>119</sup>), a tetrazole group, an amino group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted amino group (-NHR<sup>120</sup>; -NR<sup>121</sup>R<sup>122</sup>); and
- which, independently of each other, can be substituted with one or more substituents, which can be the same or different; and,
- wherein optionally, the pairs R<sup>106</sup>/R<sup>107</sup>, R<sup>110</sup>/R<sup>111</sup>, R<sup>114</sup>/R<sup>115</sup>, R<sup>116</sup>/R<sup>117</sup> and R<sup>121</sup>/R<sup>122</sup>, independently of each other, may form a part of a ring; and
- wherein the substituents R<sup>100</sup>, R<sup>101</sup>, R<sup>102</sup>, R<sup>103</sup>, R<sup>104</sup>, R<sup>105</sup>, R<sup>106</sup>, R<sup>107</sup>, R<sup>108</sup>, R<sup>109</sup>, R<sup>110</sup>, R<sup>111</sup>, R<sup>112</sup>, R<sup>113</sup>, R<sup>114</sup>, R<sup>115</sup>, R<sup>116</sup>, R<sup>117</sup>, R<sup>118</sup>, R<sup>119</sup>, R<sup>120</sup>, R<sup>121</sup>, and



$R^{122}$ , independently of each other are a hydrogen atom (-H), or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group;

or wherein the group PM has the formula (III)



- wherein  $X^3$  is  $CR^{131}R^{132}$ , O, S, SO,  $SO_2$ , or  $NR^{133}$ , and
- wherein  $R^{131}$ ,  $R^{132}$ , and  $R^{133}$ , independently of each other, are
- a hydrogen atom (-H); or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group or, a carbaldehyde (-CHO), a ketone group ( $-CO-R^{140}$ ), a boronic acid group ( $-B(OH)_2$ ), a cyano group ( $-C\equiv N$ ), a carboxylic acid group ( $-COOH$ ), a carboxylic acid ester group ( $-COOR^{141}$ ), a carboxylic acid anhydride group ( $-CO-O-CO-R^{142}$ ), a hydroxamic acid group ( $-CO-NH(OH)$ ), a N-substituted hydroxamic acid group ( $-CO-NR^{143}(OH)$ ), a O-substituted hydroxamic acid group ( $-CO-NH(OR^{144})$ ), a carboxamide group ( $-CO-NH_2$ ), a N-substituted or N,N-disubstituted carboxylic acid amide group, ( $-CO-NHR^{145}$ ;  $-CO-NR^{146}R^{147}$ ), an amido group ( $-HN-CO-R^{148}$ ), a sulfonic acid group ( $-SO_3H$ ), a sulfonamide group ( $-SO_2-NH_2$ ), a N-substituted or N,N-disubstituted sulfonamide group ( $-SO_2-NHR^{149}$ ;  $-SO_2-NR^{150}R^{151}$ ), an amidosulfone group ( $-NH-SO_2-R^{152}$ ), a sulfone group ( $-SO_2-R^{153}$ ), a phosphoric acid group ( $-OP(=O)(OH)_2$ ), a phosphoric acid ester group

(-OP(=O)(OR<sup>154</sup>)(OR<sup>155</sup>)), a **phosphonic acid** group (-P(=O)(OH)<sub>2</sub>), an **phosphonic acid ester** group (-P(=O)(OR<sup>156</sup>)(OR<sup>157</sup>)), a **halogen atom**, a **trifluormethyl** group (-CF<sub>3</sub>), a **thiol** group (-SH); a **thioether** group (-S-R<sup>158</sup>), a **hydroxy** group (-OH); an **alkoxy** group (-O-R<sup>159</sup>), a **tetrazole** group, an **amino** group (-NH<sub>2</sub>), or a **N-substituted** or **N,N-disubstituted amino** group (-NHR<sup>160</sup>; -NR<sup>161</sup>R<sup>162</sup>); and

- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; and,
- wherein optionally, the **the pair** R<sup>131</sup>/R<sup>132</sup>, if present, as well the pairs R<sup>146</sup>/R<sup>147</sup>, R<sup>150</sup>/R<sup>151</sup>, R<sup>154</sup>/R<sup>155</sup>, R<sup>156</sup>/R<sup>157</sup> and R<sup>161</sup>/R<sup>162</sup>, independently of each other, may form a part of a **ring**; and
- wherein the substituents R<sup>140</sup>, R<sup>141</sup>, R<sup>142</sup>, R<sup>143</sup>, R<sup>144</sup>, R<sup>145</sup>, R<sup>146</sup>, R<sup>147</sup>, R<sup>148</sup>, R<sup>149</sup>, R<sup>150</sup>, R<sup>151</sup>, R<sup>152</sup>, R<sup>153</sup>, R<sup>154</sup>, R<sup>155</sup>, R<sup>156</sup>, R<sup>157</sup>, R<sup>158</sup>, R<sup>159</sup>, R<sup>160</sup>, R<sup>161</sup>, and R<sup>162</sup>, independently of each other are a **hydrogen atom** (-H), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

wherein A<sup>2</sup> is

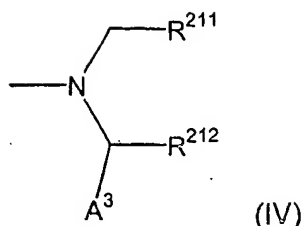
- a **hydrogen atom** (-H); or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group or, a **carbaldehyde** (-CHO), a **ketone** group (-CO-R<sup>180</sup>), a **boronic acid** group (-B(OH)<sub>2</sub>), a **cyano** group (-C≡N), a **carboxylic acid** group (-COOH), a **carboxylic acid ester** group (-COOR<sup>181</sup>), a **carboxylic acid anhydride** group (-CO-O-CO-R<sup>182</sup>), a **hydroxamic acid** group (-CO-NH(OH)), a **N-substituted hydroxamic acid** group (-CO-NR<sup>183</sup>(OH)), a **O-substituted hydroxamic acid** group (-CO-NH(OR<sup>184</sup>)), a **carboxamide** group

- (-CO-NH<sub>2</sub>), a N-substituted or N,N-disubstituted **carboxylic acid amide** group, (-CO-NHR<sup>185</sup>, -CO-NR<sup>186</sup>R<sup>187</sup>), an **amido** group (-HN-CO-R<sup>188</sup>), a **sulfonic acid** group (-SO<sub>3</sub>H), a **sulfonamide** group (-SO<sub>2</sub>-NH<sub>2</sub>), a N-substituted or N,N-disubstituted **sulfonamide** group (-SO<sub>2</sub>-NHR<sup>189</sup>, -SO<sub>2</sub>-NR<sup>190</sup>R<sup>191</sup>), an **amidosulfone** group (-NH-SO<sub>2</sub>-R<sup>192</sup>), a **sulfone** group (-SO<sub>2</sub>-R<sup>193</sup>), a **phosphoric acid** group (-OP(=O)(OH)<sub>2</sub>), a **phosphoric acid ester** group (-OP(=O)(OR<sup>194</sup>)(OR<sup>195</sup>)), a **phosphonic acid** group (-P(=O)(OH)<sub>2</sub>), an **phosphonic acid ester** group (-P(=O)(OR<sup>196</sup>)(OR<sup>197</sup>)), a **halogen atom**, a **trifluormethyl** group (-CF<sub>3</sub>), a **thiol** group (-SH); a **thioether** group (-S-R<sup>198</sup>), a **hydroxy** group (-OH); an **alkoxy** group (-O-R<sup>199</sup>), a **tetrazole** group, an **amino** group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted **amino** group (-NHR<sup>200</sup>, -NR<sup>201</sup>R<sup>202</sup>); and
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; and,
  - wherein optionally, the pairs R<sup>186</sup>/R<sup>187</sup>, R<sup>190</sup>/R<sup>191</sup>, R<sup>194</sup>/R<sup>195</sup>, R<sup>196</sup>/R<sup>197</sup> and R<sup>201</sup>/R<sup>202</sup> independently of each other, may form a part of a **ring**; and
  - wherein the substituents R<sup>180</sup>, R<sup>181</sup>, R<sup>182</sup>, R<sup>183</sup>, R<sup>184</sup>, R<sup>185</sup>, R<sup>186</sup>, R<sup>187</sup>, R<sup>188</sup>, R<sup>189</sup>, R<sup>190</sup>, R<sup>191</sup>, R<sup>192</sup>, R<sup>193</sup>, R<sup>194</sup>, R<sup>195</sup>, R<sup>196</sup>, R<sup>197</sup>, R<sup>198</sup>, R<sup>199</sup>, R<sup>200</sup>, R<sup>201</sup>, and R<sup>202</sup>, independently of each other are a **hydrogen atom** (-H), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

or wherein the group PM

has the formula (IV)

37



- wherein  $R^{211}$  and  $R^{212}$ , independently of each other, are
- a hydrogen atom (-H); or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group or, a carbaldehyde (-CHO), a ketone group (-CO-R<sup>220</sup>), a boronic acid group (-B(OH)<sub>2</sub>), a cyano group (-C≡N), a carboxylic acid group (-COOH), a carboxylic acid ester group (-COOR<sup>221</sup>), a carboxylic acid anhydride group (-CO-O-CO-R<sup>222</sup>), a hydroxamic acid group (-CO-NH(OH)), a N-substituted hydroxamic acid group (-CO-NR<sup>223</sup>(OH)), a O-substituted hydroxamic acid group (-CO-NH(OR<sup>224</sup>)), a carboxamide group (-CO-NH<sub>2</sub>), a N-substituted or N,N-disubstituted carboxylic acid amide group, (-CO-NHR<sup>225</sup>; -CO-NR<sup>226</sup>R<sup>227</sup>), an amido group (-HN-CO-R<sup>228</sup>), a sulfonic acid group (-SO<sub>3</sub>H), a sulfonamide group (-SO<sub>2</sub>-NH<sub>2</sub>), a N-substituted or N,N-disubstituted sulfonamide group (-SO<sub>2</sub>-NHR<sup>229</sup>; -SO<sub>2</sub>-NR<sup>230</sup>R<sup>231</sup>), an amidosulfone group (-NH-SO<sub>2</sub>-R<sup>232</sup>), a sulfone group (-SO<sub>2</sub>-R<sup>233</sup>), a phosphoric acid group (-OP(=O)(OH)<sub>2</sub>), a phosphoric acid ester group (-OP(=O)(OR<sup>234</sup>)(OR<sup>235</sup>)), a phosphonic acid group (-P(=O)(OH)<sub>2</sub>), an phosphonic acid ester group (-P(=O)(OR<sup>236</sup>)(OR<sup>237</sup>)), a halogen atom, a trifluormethyl group (-CF<sub>3</sub>), a thiol group (-SH); a thioether group (-S-R<sup>238</sup>), a hydroxy group (-OH); an alkoxy group (-O-R<sup>239</sup>), a tetrazole group, an amino group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted amino group (-NHR<sup>240</sup>; -NR<sup>241</sup>R<sup>242</sup>); and
- which, independently of each other, can be substituted with one or more substituents, which can be the same or different; and,

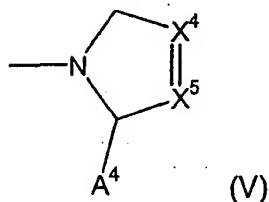
- wherein optionally, the pairs  $R^{226}/R^{227}$ ,  $R^{230}/R^{231}$ ,  $R^{234}/R^{235}$ ,  $R^{236}/R^{237}$  and  $R^{241}/R^{242}$ , independently of each other, may form a part of a ring; and
- wherein the substituents  $R^{220}$ ,  $R^{221}$ ,  $R^{222}$ ,  $R^{223}$ ,  $R^{224}$ ,  $R^{225}$ ,  $R^{226}$ ,  $R^{227}$ ,  $R^{228}$ ,  $R^{229}$ ,  $R^{230}$ ,  $R^{231}$ ,  $R^{232}$ ,  $R^{233}$ ,  $R^{234}$ ,  $R^{235}$ ,  $R^{236}$ ,  $R^{237}$ ,  $R^{238}$ ,  $R^{239}$ ,  $R^{240}$ ,  $R^{241}$ , and  $R^{242}$ , independently of each other are a hydrogen atom (-H), or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group;
- wherein  $A^3$  is
- a hydrogen atom (-H); or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group or, a carbaldehyde (-CHO), a ketone group ( $-\text{CO}-R^{260}$ ), a boronic acid group ( $-\text{B}(\text{OH})_2$ ), a cyano group ( $-\text{C}\equiv\text{N}$ ), a carboxylic acid group ( $-\text{COOH}$ ), a carboxylic acid ester group ( $-\text{COOR}^{261}$ ), a carboxylic acid anhydride group ( $-\text{CO}-\text{O}-\text{CO}-R^{262}$ ), a hydroxamic acid group ( $-\text{CO}-\text{NH}(\text{OH})$ ), a N-substituted hydroxamic acid group ( $-\text{CO}-\text{NR}^{263}(\text{OH})$ ), a O-substituted hydroxamic acid group ( $-\text{CO}-\text{NH}(\text{OR}^{264})$ ), a carboxamide group ( $-\text{CO}-\text{NH}_2$ ), a N-substituted or N,N-disubstituted carboxylic acid amide group, ( $-\text{CO}-\text{NHR}^{265}$ ;  $-\text{CO}-\text{NR}^{266}\text{R}^{267}$ ), an amido group ( $-\text{HN}-\text{CO}-R^{268}$ ), a sulfonic acid group ( $-\text{SO}_3\text{H}$ ), a sulfonamide group ( $-\text{SO}_2-\text{NH}_2$ ), a N-substituted or N,N-disubstituted sulfonamide group ( $-\text{SO}_2-\text{NHR}^{269}$ ;  $-\text{SO}_2-\text{NR}^{270}\text{R}^{271}$ ), an amidosulfone group ( $-\text{NH}-\text{SO}_2-\text{R}^{272}$ ), a sulfone group ( $-\text{SO}_2-\text{R}^{273}$ ), a phosphoric acid group ( $-\text{OP}(=\text{O})(\text{OH})_2$ ), a phosphoric acid ester group ( $-\text{OP}(=\text{O})(\text{OR}^{274})(\text{OR}^{275})$ ), a phosphonic acid group ( $-\text{P}(=\text{O})(\text{OH})_2$ ), an phosphonic acid ester group ( $-\text{P}(=\text{O})(\text{OR}^{276})(\text{OR}^{277})$ ), a halogen atom, a trifluormethyl group ( $-\text{CF}_3$ ), a thiol group ( $-\text{SH}$ ); a thioether group ( $-\text{S}-\text{R}^{278}$ ), a hydroxy group ( $-\text{OH}$ ); an alkoxy group ( $-\text{O}-\text{R}^{279}$ ), a tetrazole group, an amino

group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted **amino** group (-NHR<sup>280</sup>; -NR<sup>281</sup>R<sup>282</sup>); and

- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the pairs R<sup>266</sup>/R<sup>267</sup>, R<sup>270</sup>/R<sup>271</sup>, R<sup>274</sup>/R<sup>275</sup>, R<sup>276</sup>/R<sup>277</sup> and R<sup>281</sup>/R<sup>282</sup>, independently of each other, may form a part of a **ring**; and
- wherein the substituents R<sup>260</sup>, R<sup>261</sup>, R<sup>262</sup>, R<sup>263</sup>, R<sup>264</sup>, R<sup>265</sup>, R<sup>266</sup>, R<sup>267</sup>, R<sup>268</sup>, R<sup>269</sup>, R<sup>270</sup>, R<sup>271</sup>, R<sup>272</sup>, R<sup>273</sup>, R<sup>274</sup>, R<sup>275</sup>, R<sup>276</sup>, R<sup>277</sup>, R<sup>278</sup>, R<sup>279</sup>, R<sup>280</sup>, R<sup>281</sup>, and R<sup>282</sup>, independently of each other are a **hydrogen** atom (-H), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

or wherein the group **PM**

has the formula (V)



- wherein X<sup>4</sup> is CR<sup>291</sup> or N; and
- wherein X<sup>5</sup> is CR<sup>292</sup> or N; and
- wherein R<sup>291</sup> and R<sup>292</sup>, independently of each other, are
- a **hydrogen** atom (-H); or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**,

heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group or, a carbaldehyde (-CHO), a ketone group (-CO-R<sup>300</sup>), a boronic acid group (-B(OH)<sub>2</sub>), a cyano group (-C≡N), a carboxylic acid group (-COOH), a carboxylic acid ester group (-COOR<sup>301</sup>), a carboxylic acid anhydride group (-CO-O-CO-R<sup>302</sup>), a hydroxamic acid group (-CO-NH(OH)), a N-substituted hydroxamic acid group (-CO-NR<sup>303</sup>(OH)), a O-substituted hydroxamic acid group (-CO-NH(OR<sup>304</sup>)), a carboxamide group (-CO-NH<sub>2</sub>), a N-substituted or N,N-disubstituted carboxylic acid amide group, (-CO-NHR<sup>305</sup>; -CO-NR<sup>306</sup>R<sup>307</sup>), an amido group (-HN-CO-R<sup>308</sup>), a sulfonic acid group (-SO<sub>3</sub>H), a sulfonamide group (-SO<sub>2</sub>-NH<sub>2</sub>), a N-substituted or N,N-disubstituted sulfonamide group (-SO<sub>2</sub>-NHR<sup>309</sup>; -SO<sub>2</sub>-NR<sup>310</sup>R<sup>311</sup>), an amidosulfone group (-NH-SO<sub>2</sub>-R<sup>312</sup>), a sulfone group (-SO<sub>2</sub>-R<sup>313</sup>), a phosphoric acid group (-OP(=O)(OH)<sub>2</sub>), a phosphoric acid ester group (-OP(=O)(OR<sup>314</sup>)(OR<sup>315</sup>)), a phosphonic acid group (-P(=O)(OH)<sub>2</sub>), an phosphonic acid ester group (-P(=O)(OR<sup>316</sup>)(OR<sup>317</sup>)), a halogen atom, a trifluormethyl group (-CF<sub>3</sub>), a thiol group (-SH); a thioether group (-S-R<sup>318</sup>), a hydroxy group (-OH); an alkoxy group (-O-R<sup>319</sup>), a tetrazole group, an amino group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted amino group (-NHR<sup>320</sup>; -NR<sup>321</sup>R<sup>322</sup>); and

- which, independently of each other, can be substituted with one or more substituents, which can be the same or different; and,
- wherein optionally, the the pair R<sup>291</sup>/R<sup>292</sup>, if present, as well the pairs R<sup>306</sup>/R<sup>307</sup>, R<sup>310</sup>/R<sup>311</sup>, R<sup>314</sup>/R<sup>315</sup>, R<sup>316</sup>/R<sup>317</sup> and R<sup>321</sup>/R<sup>322</sup>, independently of each other, may form a part of a ring; and
- wherein the substituents R<sup>300</sup>, R<sup>301</sup>, R<sup>302</sup>, R<sup>303</sup>, R<sup>304</sup>, R<sup>305</sup>, R<sup>306</sup>, R<sup>307</sup>, R<sup>308</sup>, R<sup>309</sup>, R<sup>310</sup>, R<sup>311</sup>, R<sup>312</sup>, R<sup>313</sup>, R<sup>314</sup>, R<sup>315</sup>, R<sup>316</sup>, R<sup>317</sup>, R<sup>318</sup>, R<sup>319</sup>, R<sup>320</sup>, R<sup>321</sup>, and R<sup>322</sup>, independently of each other are a hydrogen atom (-H), or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl,

**heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group;**

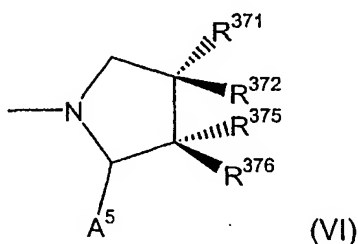
- wherein  $A^4$  is
- a hydrogen atom (-H); or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group or, a carbaldehyde (-CHO), a ketone group (-CO-R<sup>340</sup>), a boronic acid group (-B(OH)<sub>2</sub>), a cyano group (-C≡N), a carboxylic acid group (-COOH), a carboxylic acid ester group (-COOR<sup>341</sup>), a carboxylic acid anhydride group (-CO-O-CO-R<sup>342</sup>), a hydroxamic acid group (-CO-NH(OH)), a N-substituted hydroxamic acid group (-CO-NR<sup>343</sup>(OH)), a O-substituted hydroxamic acid group (-CO-NH(OR<sup>344</sup>)), a carboxamide group (-CO-NH<sub>2</sub>), a N-substituted or N,N-disubstituted carboxylic acid amide group, (-CO-NHR<sup>345</sup>; -CO-NR<sup>346</sup>R<sup>347</sup>), an amido group (-HN-CO-R<sup>348</sup>), a sulfonic acid group (-SO<sub>3</sub>H), a sulfonamide group (-SO<sub>2</sub>-NH<sub>2</sub>), a N-substituted or N,N-disubstituted sulfonamide group (-SO<sub>2</sub>-NHR<sup>349</sup>; -SO<sub>2</sub>-NR<sup>350</sup>R<sup>351</sup>), an amidosulfone group (-NH-SO<sub>2</sub>-R<sup>352</sup>), a sulfone group (-SO<sub>2</sub>-R<sup>353</sup>), a phosphoric acid group (-OP(=O)(OH)<sub>2</sub>), a phosphoric acid ester group (-OP(=O)(OR<sup>354</sup>)(OR<sup>355</sup>)), a phosphonic acid group (-P(=O)(OH)<sub>2</sub>), an phosphonic acid ester group (-P(=O)(OR<sup>356</sup>)(OR<sup>357</sup>)), a halogen atom, a trifluormethyl group (-CF<sub>3</sub>), a thiol group (-SH); a thioether group (-S-R<sup>358</sup>), a hydroxy group (-OH); an alkoxy group (-O-R<sup>359</sup>), a tetrazole group, an amino group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted amino group (-NHR<sup>360</sup>; -NR<sup>361</sup>R<sup>362</sup>); and
- which, independently of each other, can be substituted with one or more substituents, which can be the same or different; and,
- wherein optionally, the pairs R<sup>346</sup>/R<sup>347</sup>, R<sup>350</sup>/R<sup>351</sup>, R<sup>354</sup>/R<sup>355</sup>, R<sup>356</sup>/R<sup>357</sup> and R<sup>361</sup>/R<sup>362</sup>, independently of each other, may form a part of a ring; and



- wherein the substituents  $R^{340}$ ,  $R^{341}$ ,  $R^{342}$ ,  $R^{343}$ ,  $R^{344}$ ,  $R^{345}$ ,  $R^{346}$ ,  $R^{347}$ ,  $R^{348}$ ,  $R^{349}$ ,  $R^{350}$ ,  $R^{351}$ ,  $R^{352}$ ,  $R^{353}$ ,  $R^{354}$ ,  $R^{355}$ ,  $R^{356}$ ,  $R^{357}$ ,  $R^{358}$ ,  $R^{359}$ ,  $R^{360}$ ,  $R^{361}$ , and  $R^{362}$ , independently of each other are a **hydrogen atom (-H)**, or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

or wherein the group PM

has the formula (VI)



- wherein  $R^{371}$ ,  $R^{372}$ ,  $R^{375}$  and  $R^{376}$ , independently of each other, a **hydrogen atom (-H)**; or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group or, a **carbaldehyde (-CHO)**, a **ketone group (-CO- $R^{380}$ )**, a **boronic acid group (-B(OH)<sub>2</sub>)**, a **cyano group (-C≡N)**, a **carboxylic acid group (-COOH)**, a **carboxylic acid ester group (-COOR<sup>381</sup>)**, a **carboxylic acid anhydride group (-CO-O-CO-R<sup>382</sup>)**, a **hydroxamic acid group (-CO-NH(OH))**, a **N-substituted hydroxamic acid group (-CO-NR<sup>383</sup>(OH))**, a **O-substituted hydroxamic acid group (-CO-NH(OR<sup>384</sup>))**, a **carboxamide group (-CO-NH<sub>2</sub>)**, a **N-substituted or N,N-disubstituted carboxylic acid amide group, (-CO-NHR<sup>385</sup>; -CO-NR<sup>386</sup>R<sup>387</sup>)**, an **amido group (-HN-CO-R<sup>388</sup>)**, a **sulfonic acid group (-SO<sub>3</sub>H)**, a **sulfonamide group (-SO<sub>2</sub>-NH<sub>2</sub>)**, a **N-substituted or N,N-disubstituted sulfonamide group (-SO<sub>2</sub>-NHR<sup>389</sup>; -SO<sub>2</sub>-**

NR<sup>390</sup>R<sup>391</sup>), an **amidosulfone** group (-NH-SO<sub>2</sub>-R<sup>392</sup>), a **sulfone** group (-SO<sub>2</sub>-R<sup>393</sup>), a **phosphoric acid** group (-OP(=O)(OH)<sub>2</sub>), a **phosphoric acid ester** group (-OP(=O)(OR<sup>394</sup>)(OR<sup>395</sup>)), a **phosphonic acid** group (-P(=O)(OH)<sub>2</sub>), an **phosphonic acid ester** group (-P(=O)(OR<sup>396</sup>)(OR<sup>397</sup>)), a **halogen atom**, a **trifluormethyl** group (-CF<sub>3</sub>), a **thiol** group (-SH); a **thioether** group (-S-R<sup>398</sup>), a **hydroxy** group (-OH); an **alkoxy** group (-O-R<sup>399</sup>), a **tetrazole** group, an **amino** group (-NH<sub>2</sub>), or a **N-substituted** or **N,N-disubstituted amino** group (-NHR<sup>400</sup>; -NR<sup>401</sup>R<sup>402</sup>); and

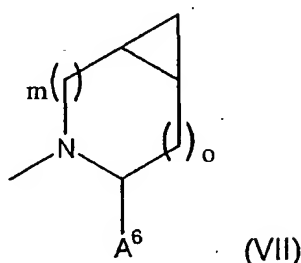
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, any **two of the groups** R<sup>371</sup>, R<sup>372</sup>, R<sup>375</sup>, and R<sup>376</sup>, as well as the pairs R<sup>386</sup>/R<sup>387</sup>, R<sup>390</sup>/R<sup>391</sup>, R<sup>394</sup>/R<sup>395</sup>, R<sup>396</sup>/R<sup>397</sup> and R<sup>401</sup>/R<sup>402</sup>, independently of each other, may form a part of a **ring**; and
  - wherein the substituents R<sup>380</sup>, R<sup>381</sup>, R<sup>382</sup>, R<sup>383</sup>, R<sup>384</sup>, R<sup>385</sup>, R<sup>386</sup>, R<sup>387</sup>, R<sup>388</sup>, R<sup>389</sup>, R<sup>390</sup>, R<sup>391</sup>, R<sup>392</sup>, R<sup>393</sup>, R<sup>394</sup>, R<sup>395</sup>, R<sup>396</sup>, R<sup>397</sup>, R<sup>398</sup>, R<sup>399</sup>, R<sup>400</sup>, R<sup>401</sup>, and R<sup>402</sup>, independently of each other are a **hydrogen atom** (-H), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group; or
- alternatively; the two groups R<sup>371</sup> and R<sup>372</sup> can be together an **oxo** (=O) or **hydroxyimino** (=N-OH) group; and
- alternatively; the two groups R<sup>375</sup> and R<sup>376</sup> can be together an **oxo** (=O) or **hydroxyimino** (=N-OH) group; and
- wherein A<sup>5</sup> is

- a hydrogen atom (-H); or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group or, a carbaldehyde (-CHO), a ketone group (-CO-R<sup>420</sup>), a boronic acid group (-B(OH)<sub>2</sub>), a cyano group (-C≡N), a carboxylic acid group (-COOH), a carboxylic acid ester group (-COOR<sup>421</sup>), a carboxylic acid anhydride group (-CO-O-CO-R<sup>422</sup>), a hydroxamic acid group (-CO-NH(OH)), a N-substituted hydroxamic acid group (-CO-NR<sup>423</sup>(OH)), a O-substituted hydroxamic acid group (-CO-NH(OR<sup>424</sup>)), a carboxamide group (-CO-NH<sub>2</sub>), a N-substituted or N,N-disubstituted carboxylic acid amide group, (-CO-NHR<sup>425</sup>; -CO-NR<sup>426</sup>R<sup>427</sup>), an amido group (-HN-CO-R<sup>428</sup>), a sulfonic acid group (-SO<sub>3</sub>H), a sulfonamide group (-SO<sub>2</sub>-NH<sub>2</sub>), a N-substituted or N,N-disubstituted sulfonamide group (-SO<sub>2</sub>-NHR<sup>429</sup>; -SO<sub>2</sub>-NR<sup>430</sup>R<sup>431</sup>), an amidosulfone group (-NH-SO<sub>2</sub>-R<sup>432</sup>), a sulfone group (-SO<sub>2</sub>-R<sup>433</sup>), a phosphoric acid group (-OP(=O)(OH)<sub>2</sub>), a phosphoric acid ester group (-OP(=O)(OR<sup>434</sup>)(OR<sup>435</sup>)), a phosphonic acid group (-P(=O)(OH)<sub>2</sub>), a phosphonic acid ester group (-P(=O)(OR<sup>436</sup>)(OR<sup>437</sup>)), a halogen atom, a trifluormethyl group (-CF<sub>3</sub>), a thiol group (-SH); a thioether group (-S-R<sup>438</sup>), a hydroxy group (-OH); an alkoxy group (-O-R<sup>439</sup>), a tetrazole group, an amino group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted amino group (-NHR<sup>440</sup>; -NR<sup>441</sup>R<sup>442</sup>); and
- which, independently of each other, can be substituted with one or more substituents, which can be the same or different; and,
- wherein optionally, the pairs R<sup>426</sup>/R<sup>427</sup>, R<sup>430</sup>/R<sup>431</sup>, R<sup>434</sup>/R<sup>435</sup>, R<sup>436</sup>/R<sup>437</sup> and R<sup>441</sup>/R<sup>442</sup>, independently of each other, may form a part of a ring; and
- wherein the substituents R<sup>420</sup>, R<sup>421</sup>, R<sup>422</sup>, R<sup>423</sup>, R<sup>424</sup>, R<sup>425</sup>, R<sup>426</sup>, R<sup>427</sup>, R<sup>428</sup>, R<sup>429</sup>, R<sup>430</sup>, R<sup>431</sup>, R<sup>432</sup>, R<sup>433</sup>, R<sup>434</sup>, R<sup>435</sup>, R<sup>436</sup>, R<sup>437</sup>, R<sup>438</sup>, R<sup>439</sup>, R<sup>440</sup>, R<sup>441</sup>, and R<sup>442</sup>, independently of each other are a hydrogen atom (-H), or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl,

**heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group;**

or wherein the group PM

has the formula (VII)



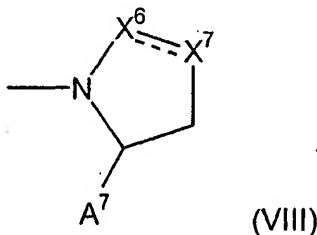
- wherein m is equal to 1 or 2, and o is equal to 1 or 2, and m or o can be 0;
- wherein A<sup>6</sup> is a **hydrogen atom (-H)**; or an **alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl** group or, a **carbaldehyde (-CHO)**, a **ketone group (-CO-R<sup>460</sup>)**, a **boronic acid group (-B(OH)<sub>2</sub>)**, a **cyano group (-C≡N)**, a **carboxylic acid group (-COOH)**, a **carboxylic acid ester group (-COOR<sup>461</sup>)**, a **carboxylic acid anhydride group (-CO-O-CO-R<sup>462</sup>)**, a **hydroxamic acid group (-CO-NH(OH))**, a **N-substituted hydroxamic acid group (-CO-NR<sup>463</sup>(OH))**, a **O-substituted hydroxamic acid group (-CO-NH(OR<sup>464</sup>))**, a **carboxamide group (-CO-NH<sub>2</sub>)**, a **N-substituted or N,N-disubstituted carboxylic acid amide group, (-CO-NHR<sup>465</sup>; -CO-NR<sup>466</sup>R<sup>467</sup>)**, an **amido group (-HN-CO-R<sup>468</sup>)**, a **sulfonic acid group (-SO<sub>3</sub>H)**, a **sulfonamide group (-SO<sub>2</sub>-NH<sub>2</sub>)**, a **N-substituted or N,N-disubstituted sulfonamide group (-SO<sub>2</sub>-NHR<sup>469</sup>; -SO<sub>2</sub>-NR<sup>470</sup>R<sup>471</sup>)**, an **amidosulfone group (-NH-SO<sub>2</sub>-R<sup>472</sup>)**, a **sulfone group (-SO<sub>2</sub>-R<sup>473</sup>)**, a **phosphoric acid group (-OP(=O)(OH)<sub>2</sub>)**, a **phosphoric acid ester group**

(-OP(=O)(OR<sup>474</sup>)(OR<sup>475</sup>)), a **phosphonic acid** group (-P(=O)(OH)<sub>2</sub>), an **phosphonic acid ester** group (-P(=O)(OR<sup>476</sup>)(OR<sup>477</sup>)), a **halogen atom**, a **trifluormethyl** group (-CF<sub>3</sub>), a **thiol** group (-SH); a **thioether** group (-S-R<sup>478</sup>), a **hydroxy** group (-OH); an **alkoxy** group (-O-R<sup>479</sup>), a **tetrazole** group, an **amino** group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted **amino** group (-NHR<sup>480</sup>; -NR<sup>481</sup>R<sup>482</sup>);

- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the pairs R<sup>466</sup>/R<sup>467</sup>, R<sup>470</sup>/R<sup>471</sup>, R<sup>474</sup>/R<sup>475</sup>, R<sup>476</sup>/R<sup>477</sup> and R<sup>481</sup>/R<sup>482</sup>, independently of each other, may form a part of a **ring**; and
- wherein the substituents R<sup>460</sup>, R<sup>461</sup>, R<sup>462</sup>, R<sup>463</sup>, R<sup>464</sup>, R<sup>465</sup>, R<sup>466</sup>, R<sup>467</sup>, R<sup>468</sup>, R<sup>469</sup>, R<sup>470</sup>, R<sup>471</sup>, R<sup>472</sup>, R<sup>473</sup>, R<sup>474</sup>, R<sup>475</sup>, R<sup>476</sup>, R<sup>477</sup>, R<sup>478</sup>, R<sup>479</sup>, R<sup>480</sup>, R<sup>481</sup>, and R<sup>482</sup>, independently of each other are a **hydrogen atom** (-H), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

**or wherein the group PM**

has the formula (VIII)



- wherein  $X^6$  is selected from  $CR^{490}R^{491}$ , O, S or  $NR^{492}$ , when the bond between  $X^6$  and  $X^7$  is a single bond; and
- wherein  $X^7$  is selected from  $CR^{493}R^{494}$ , O, S, or  $NR^{495}$ , when the bond between  $X^6$  and  $X^7$  is a single bond;
- or alternatively,
- wherein  $X^6$  is selected from  $CR^{496}$  or N, when the bond between  $X^6$  and  $X^7$  is a double bond; and
- wherein  $X^7$  is selected from  $CR^{497}$  or N, when the bond between  $X^6$  and  $X^7$  is a double bond; and
- wherein  $R^{490}$ ,  $R^{491}$ ,  $R^{492}$ ,  $R^{493}$ ,  $R^{494}$ ,  $R^{495}$ ,  $R^{496}$ , and  $R^{497}$ , independently of each other, are a **hydrogen atom** (-H); or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group or, a **carbaldehyde** (-CHO), a **ketone** group (-CO- $R^{500}$ ), a **boronic acid** group (-B(OH)<sub>2</sub>), a **cyano** group (-C≡N), a **carboxylic acid** group (-COOH), a **carboxylic acid ester** group (-COOR<sup>501</sup>), a **carboxylic acid anhydride** group (-CO-O-CO- $R^{502}$ ), a **hydroxamic acid** group (-CO-NH(OH)), a **N-substituted hydroxamic acid** group (-CO-NR<sup>503</sup>(OH)), a **O-substituted hydroxamic acid** group (-CO-NH(OR<sup>504</sup>)), a **carboxamide** group (-CO-NH<sub>2</sub>), a **N-substituted or N,N-disubstituted carboxylic acid amide** group, (-CO-NHR<sup>505</sup>; -CO-NR<sup>506</sup>R<sup>507</sup>), an **amido** group (-HN-CO- $R^{508}$ ), a **sulfonic acid** group (-SO<sub>3</sub>H), a **sulfonamide** group (-SO<sub>2</sub>-NH<sub>2</sub>), a **N-substituted or N,N-disubstituted sulfonamide** group (-SO<sub>2</sub>-NHR<sup>509</sup>; -SO<sub>2</sub>-NR<sup>510</sup>R<sup>511</sup>), an **amidosulfone** group (-NH-SO<sub>2</sub>- $R^{512}$ ), a **sulfone** group (-SO<sub>2</sub>- $R^{513}$ ), a **phosphoric acid** group (-OP(=O)(OH)<sub>2</sub>), a **phosphoric acid ester** group (-OP(=O)(OR<sup>514</sup>)(OR<sup>515</sup>)), a **phosphonic acid** group (-P(=O)(OH)<sub>2</sub>), an **phosphonic acid ester** group (-P(=O)(OR<sup>516</sup>)(OR<sup>517</sup>)), a **halogen atom**, a **trifluormethyl** group (-CF<sub>3</sub>), a **thiol** group (-SH); a **thioether** group (-S- $R^{518}$ ), a **hydroxy** group (-OH); an **alkoxy** group (-O- $R^{519}$ ), a **tetrazole** group, an **amino**

group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted **amino** group (-NHR<sup>520</sup>; -NR<sup>521</sup>R<sup>522</sup>); and

- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, any two the groups R<sup>490</sup>, R<sup>491</sup>, R<sup>492</sup>, R<sup>493</sup>, R<sup>494</sup>, R<sup>495</sup>, R<sup>496</sup>, and R<sup>497</sup>, if present, as well as the pairs R<sup>506</sup>/R<sup>507</sup>, R<sup>510</sup>/R<sup>511</sup>, R<sup>514</sup>/R<sup>515</sup>, R<sup>516</sup>/R<sup>517</sup> and R<sup>521</sup>/R<sup>522</sup>, independently of each other, may form a part of a ring; and
- wherein the substituents R<sup>500</sup>, R<sup>501</sup>, R<sup>502</sup>, R<sup>503</sup>, R<sup>504</sup>, R<sup>505</sup>, R<sup>506</sup>, R<sup>507</sup>, R<sup>508</sup>, R<sup>509</sup>, R<sup>510</sup>, R<sup>511</sup>, R<sup>512</sup>, R<sup>513</sup>, R<sup>514</sup>, R<sup>515</sup>, R<sup>516</sup>, R<sup>517</sup>, R<sup>518</sup>, R<sup>519</sup>, R<sup>520</sup>, R<sup>521</sup>, and R<sup>522</sup>, independently of each other are a **hydrogen** atom (-H), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group; and
- wherein A<sup>7</sup> is
- a **hydrogen** atom (-H); or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group or, a **carbaldehyde** (-CHO), a **ketone** group (-CO-R<sup>540</sup>), a **boronic acid** group (-B(OH)<sub>2</sub>), a **cyano** group (-C≡N), a **carboxylic acid** group (-COOH), a **carboxylic acid ester** group (-COOR<sup>541</sup>), a **carboxylic acid anhydride** group (-CO-O-CO-R<sup>542</sup>), a **hydroxamic acid** group (-CO-NH(OH)), a **N-substituted hydroxamic acid** group (-CO-NR<sup>543</sup>(OH)), a **O-substituted hydroxamic acid** group (-CO-NH(OR<sup>544</sup>)), a **carboxamide** group (-CO-NH<sub>2</sub>), a **N-substituted or N,N-disubstituted carboxylic acid amide** group, (-CO-NHR<sup>545</sup>; -CO-NR<sup>546</sup>R<sup>547</sup>), an **amido** group (-HN-CO-R<sup>548</sup>), a **sulfonic acid** group (-SO<sub>3</sub>H), a **sulfonamide** group (-SO<sub>2</sub>-NH<sub>2</sub>), a **N-substituted or N,N-disubstituted sulfonamide** group (-SO<sub>2</sub>-NHR<sup>549</sup>; -SO<sub>2</sub>-NR<sup>550</sup>R<sup>551</sup>), an **amidosulfone** group (-NH-SO<sub>2</sub>-R<sup>552</sup>), a **sulfone** group (-SO<sub>2</sub>-R<sup>553</sup>), a **phosphoric**

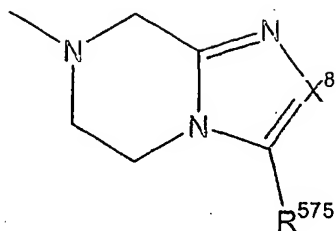
**acid group** ( $-\text{OP}(=\text{O})(\text{OH})_2$ ), a **phosphoric acid ester group** ( $-\text{OP}(=\text{O})(\text{OR}^{554})(\text{OR}^{555})$ ), a **phosphonic acid group** ( $-\text{P}(=\text{O})(\text{OH})_2$ ), an **phosphonic acid ester group** ( $-\text{P}(=\text{O})(\text{OR}^{556})(\text{OR}^{557})$ ), a **halogen atom**, a **trifluormethyl group** ( $-\text{CF}_3$ ), a **thiol group** ( $-\text{SH}$ ); a **thioether group** ( $-\text{S}-\text{R}^{558}$ ), a **hydroxy group** ( $-\text{OH}$ ); an **alkoxy group** ( $-\text{O}-\text{R}^{559}$ ), a **tetrazole group**, an **amino group** ( $-\text{NH}_2$ ), or a **N-substituted or N,N-disubstituted amino group** ( $-\text{NHR}^{560}$ ;  $-\text{NR}^{561}\text{R}^{562}$ ); and

- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the pairs  $\text{R}^{546}/\text{R}^{547}$ ,  $\text{R}^{550}/\text{R}^{551}$ ,  $\text{R}^{554}/\text{R}^{555}$ ,  $\text{R}^{556}/\text{R}^{557}$  and  $\text{R}^{561}/\text{R}^{562}$ , independently of each other, may form a part of a **ring**; and
- wherein the substituents  $\text{R}^{540}$ ,  $\text{R}^{541}$ ,  $\text{R}^{542}$ ,  $\text{R}^{543}$ ,  $\text{R}^{544}$ ,  $\text{R}^{545}$ ,  $\text{R}^{546}$ ,  $\text{R}^{547}$ ,  $\text{R}^{548}$ ,  $\text{R}^{549}$ ,  $\text{R}^{550}$ ,  $\text{R}^{551}$ ,  $\text{R}^{552}$ ,  $\text{R}^{553}$ ,  $\text{R}^{554}$ ,  $\text{R}^{555}$ ,  $\text{R}^{556}$ ,  $\text{R}^{557}$ ,  $\text{R}^{558}$ ,  $\text{R}^{559}$ ,  $\text{R}^{560}$ ,  $\text{R}^{561}$ , and  $\text{R}^{562}$ , independently of each other are a **hydrogen atom** ( $-\text{H}$ ), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

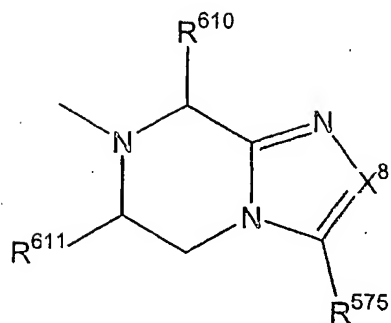
**or wherein the group PM**

**has the formula (IX) or (IXa)**





(IX)



(IXa)

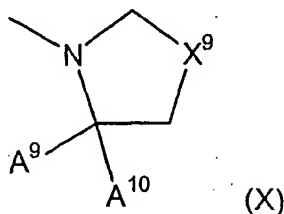
- wherein  $X^8$  is N or  $CR^{570}$ ; and
- wherein  $R^{570}$ ,  $R^{575}$ ,  $R^{610}$  and  $R^{611}$  independently of each other, are  
a hydrogen atom (-H); or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group or, a carbaldehyde (-CHO), a ketone group (-CO- $R^{580}$ ), a boronic acid group ( $-B(OH)_2$ ), a cyano group ( $-C\equiv N$ ), a carboxylic acid group (-COOH), a carboxylic acid ester group ( $-COOR^{581}$ ), a carboxylic acid anhydride group ( $-CO-O-CO-R^{582}$ ), a hydroxamic acid group ( $-CO-NH(OH)$ ), a N-substituted hydroxamic acid group ( $-CO-NR^{583}(OH)$ ), a O-substituted hydroxamic acid group ( $-CO-NH(OR^{584})$ ), a carboxamide group (-CO-NH<sub>2</sub>), a N-substituted or N,N-disubstituted carboxylic acid amide group, ( $-CO-NHR^{585}$ ;  $-CO-NR^{586}R^{587}$ ), an amido group ( $-HN-CO-R^{588}$ ), a sulfonic acid group ( $-SO_3H$ ), a sulfonamide group ( $-SO_2-NH_2$ ), a N-substituted or N,N-disubstituted sulfonamide group ( $-SO_2-NHR^{589}$ ;  $-SO_2-NR^{590}R^{591}$ ), an amidosulfone group ( $-NH-SO_2-R^{592}$ ), a sulfone group ( $-SO_2-R^{593}$ ), a phosphoric acid group ( $-OP(=O)(OH)_2$ ), a phosphoric acid ester group ( $-OP(=O)(OR^{594})(OR^{595})$ ), a phosphonic acid group ( $-P(=O)(OH)_2$ ), an phosphonic acid ester group ( $-P(=O)(OR^{596})(OR^{597})$ ), a halogen atom, a trifluormethyl group ( $-CF_3$ ), a thiol group (-SH); a thioether group ( $-S-R^{598}$ ), a hydroxy group (-OH); an alkoxy group ( $-O-R^{599}$ ), a tetrazole group, an amino

group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted **amino** group (-NHR<sup>600</sup>; -NR<sup>601</sup>R<sup>602</sup>);

- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the pairs R<sup>570</sup>/R<sup>575</sup>, if present, as well as the pairs R<sup>586</sup>/R<sup>587</sup>, R<sup>590</sup>/R<sup>591</sup>, R<sup>594</sup>/R<sup>595</sup>, R<sup>596</sup>/R<sup>597</sup> and R<sup>601</sup>/R<sup>602</sup>, independently of each other, may form a part of a **ring**; and
- wherein the substituents R<sup>580</sup>, R<sup>581</sup>, R<sup>582</sup>, R<sup>583</sup>, R<sup>584</sup>, R<sup>585</sup>, R<sup>586</sup>, R<sup>587</sup>, R<sup>588</sup>, R<sup>589</sup>, R<sup>590</sup>, R<sup>591</sup>, R<sup>592</sup>, R<sup>593</sup>, R<sup>594</sup>, R<sup>595</sup>, R<sup>596</sup>, R<sup>597</sup>, R<sup>598</sup>, R<sup>599</sup>, R<sup>600</sup>, R<sup>601</sup>, and R<sup>602</sup>, independently of each other are a **hydrogen** atom (-H), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

or wherein the group **PM**

has the formula (X)



- wherein the groups X<sup>9</sup> is CR<sup>900</sup>R<sup>901</sup>, S, SO, SO<sub>2</sub> or NR<sup>902</sup>
  - wherein R<sup>900</sup>, R<sup>901</sup> and R<sup>902</sup>, are, independently of each other, selected from hydrogen, fluorine, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, which is linear or branched

and is optionally substituted with 1, 2, 3, 4, or 5 halogens, or  
-C(=O)NR<sup>910</sup>R<sup>911</sup>.

- wherein A<sup>9</sup> and A<sup>10</sup> are, independently of each other, selected from hydrogen, cyano, -C(=O)NR<sup>912</sup>R<sup>913</sup>, or C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein

- R<sup>910</sup> and R<sup>912</sup>, are, independently of each other, selected from hydrogen, or C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens; and
- R<sup>911</sup> and R<sup>913</sup>, are, independently of each other, selected from the group consisting of

(1) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5, substituents independently selected from halogen and R<sup>920</sup>;

(2) C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6 or 7 substituents independently selected from (a) 0, 1, 2, 3, 4, or 5 halogens, and (b) 0, 1, 2 substituents selected from the group consisting of

- (a) hydroxy,
- (b) -COOH,
- (c) -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester,
- (d) phenyl,
- (e) naphthyl,
- (f) C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl,
- (g) a 5 - or 6 membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur;
- (h) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (a) two fused heterocyclic rings, each

heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (b) a benzene ring fused to a 5- or 6-membered heterocycle having 1, 2, or 3 hetero atoms;

- wherein said C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl, phenyl, naphthyl, are optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from halogen and R<sup>920</sup>, and said 5 or 6 membered heterocycle and said 8, 9 or 10 - membered bicyclic ring system are each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, and R<sup>920</sup>; and

(3) C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, which is optionally substituted with 1, 2, or 3 groups independently selected from halogen, hydroxy, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein R<sup>920</sup> is selected from the group consisting of:

(1) hydroxy;

(2) cyano;

(3) C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl optionally substituted with 1, 2, or 3 groups independently selected from halogen, hydroxy, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, wherein said -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl are linear or branched and are optionally substituted with 1, 2, 3, 4, 5 or 6 substituents selected from 1, 2, 3, 4, or 5 halogens, and 0 or 1 substituents selected from -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, -COOH, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl substituents being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(4) C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub>, C<sub>9</sub> or C<sub>10</sub> alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6, or 7 substituents independently selected from 0, 1, 2, 3, 4, or 5 halogen atoms and 0, 1, or 2 groups selected from

- (a) hydroxy;
- (b) -COOH;
- (c) -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, which may linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens;
- (d) a 5- or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.;
- (e) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (i) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (ii) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;
- (f) -CONR<sup>925</sup>R<sup>925</sup>;
- (g) -SO<sub>2</sub>NR<sup>925</sup>R<sup>925</sup>;
- (h) -NR<sup>925</sup>-C(=O)R<sup>925</sup>;
- (i) -NR<sup>925</sup>-C(=O)NR<sup>925</sup>R<sup>925</sup>;

(j)  $-\text{NR}^{925}\text{COOR}^{930}$

(k)  $-\text{O}-\text{CO}-\text{R}^{930}$

(l)  $-\text{O}-\text{CO}-\text{NR}^{925}\text{R}^{925}$ ;

(m)  $-\text{NR}^{925}\text{SO}_2\text{R}^{930}$ ;

(n)  $-\text{NR}^{925}\text{R}^{925}$ ;

(o) phenyl which is optionally substituted with 1, 2, 3, 4, or 5 group independently selected from halogen, hydroxy,  $\text{C}_1$ ,  $\text{C}_2$ ,  $\text{C}_3$ ,  $\text{C}_4$ ,  $\text{C}_5$  or  $\text{C}_6$  alkyl,  $-\text{OC}_1$ ,  $-\text{OC}_2$ ,  $-\text{OC}_3$ ,  $-\text{OC}_4$ ,  $-\text{OC}_5$  or  $-\text{OC}_6$  alkyl,  $-\text{COOH}$ ,  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester, said  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  alkyl,  $-\text{OC}_1$ ,  $-\text{OC}_2$ ,  $-\text{OC}_3$ ,  $-\text{OC}_4$ ,  $-\text{OC}_5$  or  $-\text{OC}_6$  alkyl,  $-\text{COOH}$ ,  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, 5, or 6 substituents independently selected from 0 or 1  $\text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  cycloalkyl and 0, 1, 2, 3, 4, or 5 halogens, and

(p)  $\text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  cycloalkyl, which is optionally substituted with 1, 2, 3, 4, 5, or 6 halogens;

(5)  $\text{OC}_1, \text{OC}_2, \text{OC}_3, \text{OC}_4, \text{OC}_5, \text{OC}_6, \text{OC}_7, \text{OC}_8, \text{OC}_9$  or  $\text{OC}_{10}$  alkyl, which is linear or branched and is optionally substituted with 0, 1, 2, 3, 4, or 5 halogen atoms and 0, 1, or 2 substituents selected from

(a) hydroxy;

(b)  $-\text{COOH}$ ;

(c)  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester, which may be linear or branched and is optionally substituted with 1, 2, 3, 4 or 5 halogens;

(d) a 5 - or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen,  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5$  or  $-\text{OC}_6$  alkyl, said  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5$  or  $-\text{OC}_6$  alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.;

(e) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (i) two fused heterocyclic rings, each

heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (ii) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(f) -CONR<sup>925</sup>R<sup>925</sup>;

(g) -SO<sub>2</sub>NR<sup>925</sup>R<sup>925</sup>;

(h) -NR<sup>925</sup>-C(=O)R<sup>925</sup>;

(i) -NR<sup>925</sup>-C(=O)NR<sup>925</sup>R<sup>925</sup>;

(j) -NR<sup>925</sup>COOR<sup>930</sup>;

(k) -O-CO-R<sup>930</sup>;

(l) -O-CO-NR<sup>925</sup>R<sup>925</sup>;

(m) -NR<sup>925</sup>SO<sub>2</sub>R<sup>930</sup>;

(n) -NR<sup>925</sup>R<sup>925</sup>;

(o) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5 groups independently selected from halogen, hydroxy, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, 5, or 6 substituents independently selected from 0 or 1 C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl and 0, 1, 2, 3, 4, or 5 halogens, and

(p) C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl, which is optionally substituted with 1, 2, 3, 4, 5, or 6 halogens;

(6) -COOH;

(7) -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, which may be linear or branched and is optionally substituted with 1, 2, 3, 4, 5 halogens;

(8) a 5 - or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, said heterocycle being optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.

(9) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (a) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (b) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(10) -CONR<sup>925</sup>R<sup>925</sup>;

(11) -SO<sub>2</sub>NR<sup>925</sup>R<sup>925</sup>;

(12) -NR<sup>925</sup>-C(=O)R<sup>925</sup>;

(13) -NR<sup>925</sup>-C(=O)NR<sup>925</sup>R<sup>925</sup>;

(14) -NR<sup>925</sup>COOR<sup>930</sup>

(15) -O-CO-R<sup>930</sup>

(16) -O-CO-NR<sup>925</sup>R<sup>925</sup>;

(17) -NR<sup>925</sup>SO<sub>2</sub>R<sup>930</sup>;

(18) -NR<sup>925</sup>R<sup>925</sup>;

(19) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5 group independently selected from halogen, hydroxy, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>,



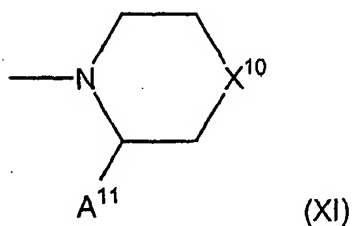
-OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein R<sup>930</sup> is selected from the group consisting of phenyl, C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, and C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, wherein C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6, substituents independently selected from 0, 1, 2, 3, 4, or 5 halogens, 0 or 1 phenyl, wherein said optional phenyl substituent and said R<sup>930</sup>, when R<sup>930</sup> is phenyl or C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, are optionally substituted with 1, 2, 3, 4, or 5 substituents, independently selected from halogen, OH, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, or C<sub>5</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, or -OC<sub>5</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, or C<sub>5</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, or -OC<sub>5</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.

wherein R<sup>925</sup> is selected from R<sup>930</sup> and hydrogen.

wherein the group PM

has the formula (XI)



- wherein the groups X<sup>10</sup> is CR<sup>1000</sup>R<sup>1001</sup>, S, SO, SO<sub>2</sub> or NR<sup>1002</sup>
- wherein R<sup>1000</sup>, R<sup>1001</sup> and R<sup>1002</sup>, are, independently of each other, selected from hydrogen, fluorine, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, which is linear or

branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens, or  
 $-C(=O)NR^{910}R^{911}$ .

and  $A^{11}$  is selected from

hydrogen, cyano,  $-C(=O)NR^{1012}R^{1013}$ , or  $C_1, C_2, C_3, C_4, C_5$  or  $C_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein

- $R^{1010}$  and  $R^{1012}$ , are, independently of each other, selected from hydrogen, or  $C_1, C_2, C_3, C_4, C_5$  or  $C_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens; and
- $R^{1011}$  and  $R^{1013}$ , are, independently of each other, selected from the group consisting of

(1) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5, substituents independently selected from halogen and  $R^{1020}$ ;

(2)  $C_1, C_2, C_3, C_4, C_5$  or  $C_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6 or 7 substituents independently selected from

(a) 0, 1, 2, 3, 4, or 5 halogens, and (b) 0, 1, 2 substituents selected from the group consisting of

(a) hydroxy,

(b)  $-COOH$ ,

(c)  $-COO(C_1, C_2, C_3, C_4, C_5$  or  $C_6$  alkyl), i.e. ester,

(d) phenyl,

(e) naphthyl,

(f)  $C_3, C_4, C_5$  or  $C_6$  cycloalkyl,

(g) a 5 - or 6 membered htereocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 heteroatoms independently selected from nitrogen , oxygen or sulfur;

(h) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (a) two fused heterocyclic rings, each

heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (b) a benzene ring fused to a 5- or 6-membered heterocycle having 1, 2, or 3 hetero atoms;

- wherein said C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl, phenyl, naphthyl, are optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from halogen and R<sup>1020</sup>, and said 5 or 6 membered heterocycle and said 8, 9 or 10 - membered bicyclic ring system are each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, and R<sup>1020</sup>; and

(3) C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, which is optionally substituted with 1, 2, or 3 groups independently selected from halogen, hydroxy, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein R<sup>1020</sup> is selected from the group consisting of:

(1) hydroxy;

(2) cyano;

(3) C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl optionally substituted with 1, 2, or 3 groups independently selected from halogen, hydroxy, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, wherein said -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl are linear or branched and are optionally substituted with 1, 2, 3, 4, 5 or 6 substituents selected from 1, 2, 3, 4, or 5 halogens, and 0 or 1 substituents selected from -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, -COOH, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl substituents being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(4) C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub>, C<sub>9</sub> or C<sub>10</sub> alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6, or 7 substituents independently selected from 0, 1, 2, 3, 4, or 5 halogen atoms and 0, 1, or 2 groups selected from

(a) hydroxy;

(b) -COOH;

(c) -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, which may linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens;

(d) a 5- or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.;

(e) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (i) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (ii) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(f) -CONR<sup>1025</sup>R<sup>1025</sup>;

(g) -SO<sub>2</sub>NR<sup>1025</sup>R<sup>1025</sup>;

(h) -NR<sup>1025</sup>-C(=O)R<sup>1025</sup>

(i) -NR<sup>1025</sup>-C(=O)NR<sup>1025</sup>R<sup>1025</sup>;

(j)  $-\text{NR}^{1025}\text{COOR}^{1030}$

(k)  $-\text{O}-\text{CO}-\text{R}^{1030}$

(l)  $-\text{O}-\text{CO}-\text{NR}^{1025}\text{R}^{1025}$ ;

(m)  $-\text{NR}^{1025}\text{SO}_2\text{R}^{1030}$ ;

(n)  $-\text{NR}^{1025}\text{R}^{1025}$ ;

(o) phenyl which is optionally substituted with 1, 2, 3, 4, or 5 group independently selected from halogen, hydroxy,  $\text{C}_1$ ,  $\text{C}_2$ ,  $\text{C}_3$ ,  $\text{C}_4$ ,  $\text{C}_5$  or  $\text{C}_6$  alkyl,  $-\text{OC}_1$ ,  $-\text{OC}_2$ ,  $-\text{OC}_3$ ,  $-\text{OC}_4$ ,  $-\text{OC}_5$  or  $-\text{OC}_6$  alkyl,  $-\text{COOH}$ ,  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester, said  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  alkyl,  $-\text{OC}_1$ ,  $-\text{OC}_2$ ,  $-\text{OC}_3$ ,  $-\text{OC}_4$ ,  $-\text{OC}_5$  or  $-\text{OC}_6$  alkyl,  $-\text{COOH}$ ,  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, 5, or 6 substituents independently selected from 0 or 1  $\text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  cycloalkyl and 0, 1, 2, 3, 4, or 5 halogens, and

(p)  $\text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  cycloalkyl, which is optionally substituted with 1, 2, 3, 4, 5, or 6 halogens;

(5)  $\text{OC}_1, \text{OC}_2, \text{OC}_3, \text{OC}_4, \text{OC}_5, \text{OC}_6, \text{OC}_7, \text{OC}_8, \text{OC}_9$  or  $\text{OC}_{10}$  alkyl, which is linear or branched and is optionally substituted with 0, 1, 2, 3, 4, or 5 halogen atoms and 0, 1, or 2 substituents selected from

(a) hydroxy;

(b)  $-\text{COOH}$ ;

(c)  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester, which may be linear or branched and is optionally substituted with 1, 2, 3, 4 or 5 halogens;

(d) a 5 - or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen,  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5$  or  $-\text{OC}_6$  alkyl, said  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5$  or  $-\text{OC}_6$  alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.;

(e) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (i) two fused heterocyclic rings, each

heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (ii) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(f) -CONR<sup>1025</sup>R<sup>1025</sup>;

(g) -SO<sub>2</sub>NR<sup>1025</sup>R<sup>1025</sup>;

(h) -NR<sup>1025</sup>-C(=O)R<sup>1025</sup>;

(i) -NR<sup>1025</sup>-C(=O)NR<sup>1025</sup>R<sup>1025</sup>;

(j) -NR<sup>1025</sup>COOR<sup>1030</sup>

(k) -O-CO-R<sup>1030</sup>

(l) -O-CO-NR<sup>1025</sup>R<sup>1025</sup>;

(m) -NR<sup>1025</sup>SO<sub>2</sub>R<sup>1030</sup>;

(n) -NR<sup>1025</sup>R<sup>1025</sup>;

(o) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5 groups independently selected from halogen, hydroxy, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, 5, or 6 substituents independently selected from 0 or 1 C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl and 0, 1, 2, 3, 4, or 5 halogens, and

(p) C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl, which is optionally substituted with 1, 2, 3, 4, 5, or 6 halogens;

(6) -COOH;

(7) -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, which may be linear or branched and is optionally substituted with 1, 2, 3, 4, 5 halogens;

(8) a 5- or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, said heterocycle being optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.

(9) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (a) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (b) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(10) -CONR<sup>1025</sup>R<sup>1025</sup>;

(11) -SO<sub>2</sub>NR<sup>1025</sup>R<sup>1025</sup>;

(12) -NR<sup>1025</sup>-C(=O)R<sup>1025</sup>

(13) -NR<sup>1025</sup>-C(=O)NR<sup>1025</sup>R<sup>1025</sup>;

(14) -NR<sup>925</sup>COOR<sup>1030</sup>

(15) -O-CO-R<sup>1030</sup>

(16) -O-CO-NR<sup>1025</sup>R<sup>1025</sup>;

(17) -NR<sup>1025</sup>SO<sub>2</sub>R<sup>1030</sup>;

(18) -NR<sup>1025</sup>R<sup>1025</sup>;

(19) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5 group independently selected from halogen, hydroxy, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>,

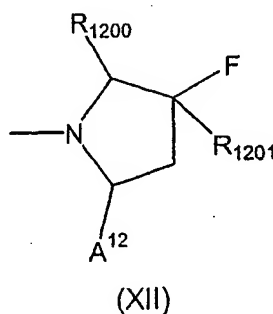
-OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein R<sup>1030</sup> is selected from the group consisting of phenyl, C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, and C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, wherein C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6, substituents independently selected from 0, 1, 2, 3, 4, or 5 halogens, 0 or 1 phenyl, wherein said optional phenyl substituent and said R<sup>930</sup>, when R<sup>930</sup> is phenyl or C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, are optionally substituted with 1, 2, 3, 4, or 5 substituents, independently selected from halogen, OH, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, or C<sub>5</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, or -OC<sub>5</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, or C<sub>5</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, or -OC<sub>5</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.

wherein R<sup>1025</sup> is selected from R<sup>1030</sup> and hydrogen.

or wherein the group PM

has the formula (XII)

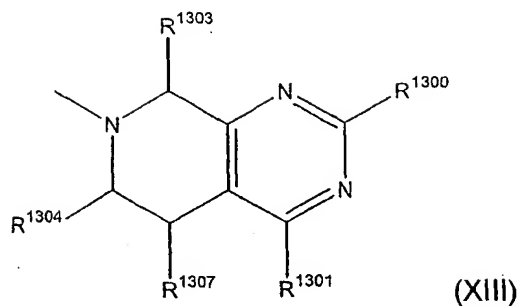


- wherein the groups R<sup>1201</sup> is hydrogen or fluoro.
- wherein R<sup>1200</sup> and A<sup>12</sup> is selected from hydrogen and cyano, and the other is hydrogen.



or wherein the group PM

has the formula XIII:



wherein:

$R^{1300}$  and  $R^{1301}$  are independently selected from the group consisting of:

- (1) hydrogen,
- (2) CN,
- (3)  $C_{1-10}$ alkyl, which is linear or branched which is unsubstituted or substituted with:
  - a) halogen, or
  - b) phenyl, which is unsubstituted or substituted with 1 - 5 substituents independently selected from halogen, CN, OH,  $R^{1302}$ ,  $OR^{1302}$ ,  $NHSO_2R^{1302}$ ,  $N(C_{1-6}alkyl)SO_2R^{1302}$ ,  $SO_2R^{1302}$ ,  $SO_2NR^{1305}R^{1306}$ ,  $NR^{1305}R^{1306}$ ,  $CONR^{1305}R^{1306}$ ,  $CO_2H$ , and  $CO_2C_{1-6}alkyl$ , wherein the  $C_{1-6}alkyl$  is linear or branched,
- (4) phenyl which is unsubstituted or substituted with 1 - 5 substituents independently selected from halogen, CN, OH,  $R^{1302}$ ,  $OR^{1302}$ ,  $NHSO_2R^{1302}$ ,  $N(C_{1-6}alkyl)SO_2R^{1302}$ ,  $SO_2R^{1302}$ ,  $SO_2NR^{1305}R^{1306}$ ,  $NR^{1305}R^{1306}$ ,  $CONR^{1305}R^{1306}$ ,  $CO_2H$ , and  $CO_2C_{1-6}alkyl$ , wherein the  $C_{1-6}alkyl$  is linear or branched,
- (5) a 5- or 6-membered heterocyclic which may be saturated or unsaturated comprising 1 - 4 heteroatoms independently selected from N, S and O, the heterocycle being unsubstituted or substituted with 1 - 3 substituents independently selected from oxo, halogen,  $NO_2$ , CN, OH,  $R^{1302}$ ,  $OR^{1302}$ ,  $NHSO_2R^{1302}$ ,  $N(C_{1-6}alkyl)SO_2R^{1302}$ ,  $SO_2R^{1302}$ ,  $SO_2NR^{1305}R^{1306}$ ,  $NR^{1305}R^{1306}$ ,

CONR<sup>1305</sup>R<sup>1306</sup>, CO<sub>2</sub>H, and CO<sub>2</sub>C<sub>1-6</sub>alkyl, wherein the C<sub>1-6</sub>alkyl is linear or branched,

(6) C<sub>3-6</sub>cycloalkyl, which is optionally substituted with 1 – 5 substituents independently selected from halogen, OH, C<sub>1-6</sub>alkyl, and OC<sub>1-6</sub>alkyl, wherein the C<sub>1-6</sub>alkyl and OC<sub>1-6</sub>alkyl are linear or branched and optionally substituted with 1 – 5 halogens,

(7) OH,

(8) OR<sup>1302</sup>, and

(9) NR<sup>1305</sup>R<sup>1306</sup>,

R<sup>1302</sup> is C<sub>1-6</sub>alkyl, which is linear or branched and which is unsubstituted or substituted with 1 – 5 groups independently selected from halogen, CO<sub>2</sub>H, and CO<sub>2</sub>C<sub>1-6</sub>alkyl, wherein the C<sub>1-6</sub>alkyl is linear or branched;

R<sup>1303</sup>, R<sup>1304</sup> and R<sup>1307</sup> are independently selected from the group consisting of:

(1) hydrogen,

(2) C<sub>1-10</sub>alkyl, which is linear or branched and which is unsubstituted or substituted with one or more substituted selected from:

a) halogen,

b) hydroxy,

c) phenyl, which is unsubstituted or substituted with 1 – 5 substituted independently selected from halogen, OH, C<sub>1-6</sub>alkyl, and OC<sub>1-6</sub>alkyl, wherein the C<sub>1-6</sub>alkyl is linear or branched and optionally substituted with 1 – 5 halogens,

d) naphthyl, wherein the naphthyl is optionally substituted with 1 – 5 substituents independently selected from halogen, OH, C<sub>1-6</sub>alkyl, and OC<sub>1-6</sub>alkyl, wherein the C<sub>1-6</sub>alkyl is linear or branched and optionally substituted with 1 – 5 halogens,

e) CO<sub>2</sub>H,

f) CO<sub>2</sub>C<sub>1-6</sub>alkyl,

g) CONR<sup>1305</sup>R<sup>1306</sup>,

- (3) CN,
- (4) phenyl which is unsubstituted or substituted with 1 – 5 substituents independently selected from C<sub>1-6</sub>alkyl, and OC<sub>1-6</sub>alkyl, hydroxy and halogen, wherein the C<sub>1-6</sub>alkyl is linear or branched and optionally substituted with 1 – 5 halogens,
- (5) naphthyl which is unsubstituted or substituted with 1 – 5 substituents independently selected from C<sub>1-6</sub>alkyl, and OC<sub>1-6</sub>alkyl, hydroxy and halogen, wherein the C<sub>1-6</sub>alkyl is linear or branched and optionally substituted with 1 – 5 halogens,
- (6) CO<sub>2</sub>H,
- (7) CO<sub>2</sub>C<sub>1-6</sub>alkyl,
- (8) CONR<sup>1305</sup>R<sup>1306</sup>, and
- (9) C<sub>3-6</sub>cycloalkyl, which is unsubstituted or substituted with 1 – 5 substituents independently selected from C<sub>1-6</sub>alkyl, and OC<sub>1-6</sub>alkyl, hydroxy and halogen, wherein the C<sub>1-6</sub>alkyl is linear or branched and optionally substituted with 1 – 5 halogens;

R<sup>1305</sup> and R<sup>1306</sup> are independently selected from the group consisting of:

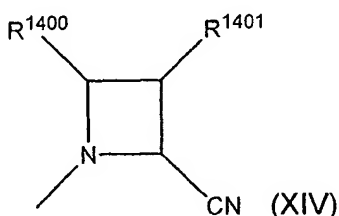
- (1) hydrogen,
- (2) phenyl, which is unsubstituted or substituted with substituents independently selected from halogen, OH, C<sub>1-6</sub>alkyl, and OC<sub>1-6</sub>alkyl, wherein the C<sub>1-6</sub>alkyl is linear or branched and optionally substituted with 1 – 5 halogens,
- (3) C<sub>3-6</sub>cycloalkyl, which is unsubstituted or substituted with 1 – 5 substituents independently selected from C<sub>1-6</sub>alkyl, and OC<sub>1-6</sub>alkyl, wherein the C<sub>1-6</sub>alkyl is linear or branched and optionally substituted with 1 – 5 halogens
- (4) C<sub>1-6</sub>alkyl, which is linear or branched and which is unsubstituted or substituted with:
  - a) halogen, or
  - b) phenyl, which is unsubstituted or substituted with 1 – 5 substituents independently selected from halogen, OH, C<sub>1-6</sub> alkyl, and OC<sub>1-6</sub>alkyl,

wherein the C<sub>1-6</sub>alkyl is linear or branched and optionally substituted with 1 – 5 halogens,

or wherein R<sup>1305</sup> and R<sup>1306</sup> together with the nitrogen atom to which they are attached form a heterocyclic ring selected from azetidine, pyrrolidine, piperidine, piperazine, and morpholine wherein said heterocyclic ring is unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, C<sub>1-6</sub>alkyl, and C<sub>1-6</sub>alkoxy, wherein alkyl and alkoxy are unsubstituted with one to five halogens;

**or wherein the group PM**

has the formula XIV:



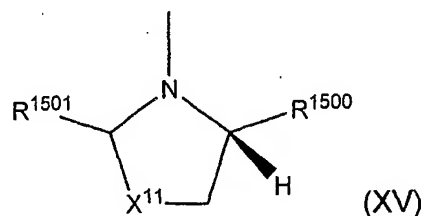
- wherein R<sup>1400</sup> and R<sup>1401</sup>, independently of each other, are
- a **hydrogen atom (-H)**; or an **alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl** group or, a **carbaldehyde (-CHO)**, a **ketone group (-CO-R<sup>1402</sup>)**, a **boronic acid group (-B(OH)<sub>2</sub>)**, a **cyano group (-C≡N)**, a **carboxylic acid group (-COOH)**, a **carboxylic acid ester group (-COOR<sup>1403</sup>)**, a **carboxylic acid anhydride group (-CO-O-CO-R<sup>1404</sup>)**, a **hydroxamic acid group (-CO-NH(OH))**, a **N-substituted hydroxamic acid group (-CO-NR<sup>1405</sup>(OH))**, a **O-substituted hydroxamic acid group (-CO-NH(OR<sup>1406</sup>))**, a **carboxamide group (-CO-NH<sub>2</sub>)**, a **N-substituted or N,N-disubstituted carboxylic acid amide group, (-CO-NHR<sup>1407</sup>, -CO-NR<sup>1408</sup>R<sup>1409</sup>)**, an **amido group (-HN-CO-R<sup>1410</sup>)**, a **sulfonic acid group (-SO<sub>3</sub>H)**, a **sulfonamide group (-SO<sub>2</sub>-NH<sub>2</sub>)**, a **N-substituted or N,N-**

disubstituted **sulfonamide** group ( $-\text{SO}_2\text{-NHR}^{1411}$ ;  $-\text{SO}_2\text{-NR}^{1412}\text{R}^{1413}$ ), an **amidosulfone** group ( $-\text{NH-SO}_2\text{-R}^{1414}$ ), a **sulfone** group ( $-\text{SO}_2\text{-R}^{1415}$ ), a **phosphoric acid** group ( $-\text{OP}(=\text{O})(\text{OH})_2$ ), a **phosphoric acid ester** group ( $-\text{OP}(=\text{O})(\text{OR}^{1416})(\text{OR}^{1417})$ ), a **phosphonic acid** group ( $-\text{P}(=\text{O})(\text{OH})_2$ ), an **phosphonic acid ester** group ( $-\text{P}(=\text{O})(\text{OR}^{1418})(\text{OR}^{1419})$ ), a **halogen atom**, a **trifluormethyl** group ( $-\text{CF}_3$ ), a **thiol** group ( $-\text{SH}$ ); a **thioether** group ( $-\text{S-R}^{1420}$ ), a **hydroxy** group ( $-\text{OH}$ ); an **alkoxy** group ( $-\text{O-R}^{1421}$ ), a **tetrazole** group, an **amino** group ( $-\text{NH}_2$ ), or a N-substituted or N,N-disubstituted **amino** group ( $-\text{NHR}^{1422}$ ;  $-\text{NR}^{1423}\text{R}^{1424}$ ); and

- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; and,
- wherein optionally, the pairs  $\text{R}^{1408}/\text{R}^{1409}$ ,  $\text{R}^{1412}/\text{R}^{1413}$ ,  $\text{R}^{1416}/\text{R}^{1417}$ ,  $\text{R}^{1418}/\text{R}^{1419}$  and  $\text{R}^{1423}/\text{R}^{1424}$ , independently of each other, may form a part of a **ring**; and
- wherein the substituents  $\text{R}^{1402}$ ,  $\text{R}^{1403}$ ,  $\text{R}^{1404}$ ,  $\text{R}^{1405}$ ,  $\text{R}^{1406}$ ,  $\text{R}^{1407}$ ,  $\text{R}^{1408}$ ,  $\text{R}^{1409}$ ,  $\text{R}^{1410}$ ,  $\text{R}^{1411}$ ,  $\text{R}^{1412}$ ,  $\text{R}^{1413}$ ,  $\text{R}^{1414}$ ,  $\text{R}^{1415}$ ,  $\text{R}^{1416}$ ,  $\text{R}^{1417}$ ,  $\text{R}^{1418}$ ,  $\text{R}^{1419}$ ,  $\text{R}^{1420}$ ,  $\text{R}^{1421}$ ,  $\text{R}^{1422}$ ,  $\text{R}^{1423}$ , and  $\text{R}^{1424}$ , independently of each other are a **hydrogen atom** ( $-\text{H}$ ), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

or wherein the group **PM**

has the formula XV:



- wherein  $X^{11}$  is  $CH_2$ ,  $CHF$  or  $CF_2$ ;
- wherein  $R^{1500}$  is selected from the group consisting of alkylcarbonyl, arylcarbonyl, cyano, heterocyclecarbonyl,  $R^{1502}R^{1503}NC(O)-$ ,  $B(OR^{1504})_2$ , (1,2,3)-dioxoborolane and 4,4,5,5-tetramethyl(1,2,3)-dioxoborolane;
- wherein  $R^{1501}$  is selected from the group consisting of alkoxyalkyl, alkyl, alkylcarbonyl, alkenyl, alkynyl, allenyl, arylalkyl, cycloalkyl, cycloalkylalkyl, cyano, haloalkyl, haloalkenyl, heterocyclealkyl, and hydroxyalkyl;
- wherein  $R^{1502}$ ,  $R^{1503}$  and  $R^{1504}$  are each independently selected from the group consisting of hydrogen, alkyl, and arylalkyl;

with the proviso that the following compounds are excluded:

glutaminy l thiazolidine (=Gln-Thia), glutaminy l pyrrolidine (=Gln-Pyrr) (from WO 03/072556), glutamin-pyrrolidin-2-carboxylic acid (= Gln-Pro), glutamin-pyrrolidin-2-carboxamid (=Gln-Pro amid), and (S,S) 4-Amino-5-(2-cyano-2,5-dihydro-pyrrol-1-yl)-6-oxo-pentanoic acid amide (Gln - 2-cyano-2,5-dihydro-pyrrolidin) (from WO 01/55105).

#### **Object of the present invention:**

It is an object of the present invention to provide DP IV inhibitor molecules with improved bioavailability resulting in a higher transport rate from intestine into blood circulation, compared with ordinary DP IV inhibitors.

A further object of the present invention is to provide inhibitor molecules for DP IV and DP IV like enzymes, which exhibit a decreased profile of side effects in comparison with ordinary DP IV inhibitors.

Furthermore, it is an object of the present invention to provide inhibitor molecules for DP IV and DP IV like enzymes with a definite half life period in the organism, wherein the half life period can be definitely controlled by administration of a further substance in combination with DP IV inhibitors. Alternatively, the problem can be

understood as an additional option which allows to control, to shorten or to prolongate the time period, during which the DP IV inhibitor is acting as an active molecule.

It is an object of the present invention to provide new DP IV inhibitors, and optionally to provide DP IV inhibitors in combination with QC inhibitors, for the manufacture of a medicament for the treatment of diseases of mammals that can be treated by modulation of DP IV- and optionally QC activity in said mammal, especially for the treatment of metabolic diseases in humans. In detail, it is the object of this invention to provide new compounds for the preparation of a medicament for the treatment of non-insulin dependent diabetes mellitus (type 2), impaired glucose tolerance, glucosuria, and disturbances of signal action at the cells of the islets of Langerhans and insulin sensitivity in the peripheral tissue in the postprandial phase of mammals, especially in humans.

Further, it is the object of this invention to provide new compounds for the preparation of a medicament for the treatment of hyperlipidemia, metabolic acidosis, diabetic neuropathy and nephropathy and of sequelae caused by diabetes mellitus in mammals; metabolism-related hypertension and cardiovascular sequelae caused by hypertension in mammals; for the prophylaxis or treatment of skin diseases and diseases of the mucosae, autoimmune diseases and inflammatory conditions, and for the prophylaxis or treatment of psychosomatic, neuropsychiatric and depressive illness, and neurodegenerative diseases such as anxiety, depression, sleep disorders, chronic fatigue, schizophrenia, epilepsy, nutritional disorders, spasm, and chronic pain, and a simple method for the treatment of those disorders.

**Solution of the problem:**

According to the invention, the first and second object is solved by use of a compound of the general formula (I), preferably having a glutaminyl or, respectively, a homoglutaminyl residue, each having both an N-unsubstituted  $\alpha$ -amino group and an unsubstituted  $\gamma$ -amido group, and more preferably by use of a L- $\alpha$ -glutaminyl or,

respectively, a L- $\alpha$ -homoglutaminyl residue according to the formulas (NH<sub>2</sub>-CO-CH<sub>2</sub>-CH<sub>2</sub>-CH(NH<sub>2</sub>)-CO-) or, respectively, (NH<sub>2</sub>-CO-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH(NH<sub>2</sub>)-CO-) as a part of the inhibitor molecules of the general formula (I).

The glutaminyl or the homoglutaminyl residue, respectively, renders the inhibitor molecule of the general formula (I) more hydrophilic than ordinary DP IV inhibitors and causes an increase of the transport rate from intestine into blood circulation by the PEPT transporter system. Thus the DP IV inhibitors according to the present invention bear the advantage to exhibit an improved bioavailability after oral uptake compared with ordinary DP IV inhibitors.

A further effect of the introduction of the glutaminyl residue into the DP IV inhibitor molecule concerning the second object of lowered side effects consists of the diminished passage through the blood brain barrier from the circulation into the central nervous system. This leads to a significantly reduced spectrum of undesired side effects of the DP IV inhibitors according to the invention.

Furthermore, it has surprisingly been found that the glutaminyl residue of the DP IV inhibitors of the general formula (I) is metabolized to a cyclic pyroglutaminyl derivative of the general formula (I), which is inactive as DP IV inhibitor *in vivo*. (see schemes 1 and 2)

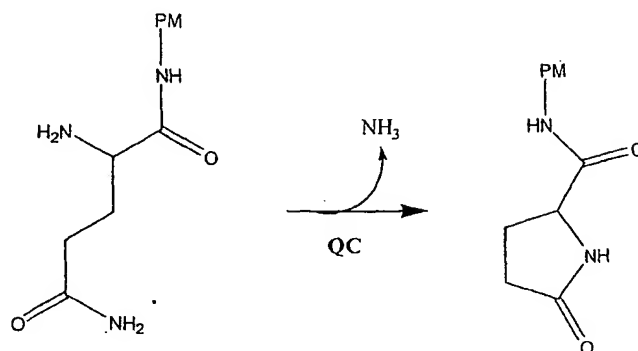
The inventors found out that this cyclisation reaction from a glutamin derivative to a pyro-glutamine derivative is accomplished enzymatically, and the responsible enzyme is glutaminyl cyclase. The enzyme glutaminyl cyclase (E.C. 2.3.2.5, abbreviated as QC) is known per se and, furthermore, as being involved in the formation of thyrotropin-releasing hormone and gonadotropin releasing hormone.

A further unexpected result was the finding that substrat specificity of glutaminyl cyclase extends also to homoglutamine. N-terminal homoglutamine as a part of a DP IV inhibitor is metabolized analogously to glutamin by glutaminyl cyclase to a cyclic

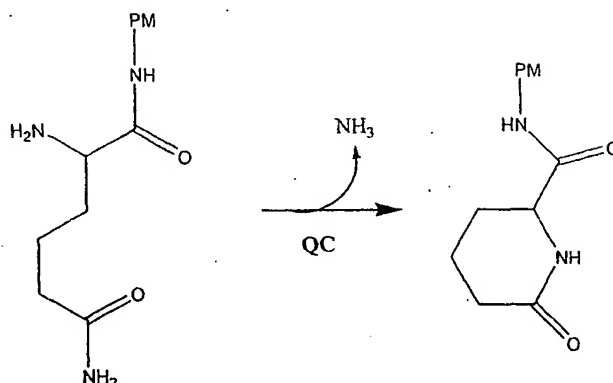


pyro-homoglutamine derivative (see reaction schemes 1 and 2 for glutamine and homoglutamine, respectively).

**Scheme 1: Cyclization of glutamine by QC**



**Scheme 2: Cyclization of homoglutamine by QC**



An action of glutaminyl cyclase on low-molecular substances, such as DP IV inhibitors according to the present invention, was not known up to the present invention, which has surprisingly detected the action of QC on DP IV inhibitors containing a glutaminyl residue, especially a L- $\alpha$ -glutaminyl residue at the N-terminus of the DP IV inhibitor according to the present invention. Furthermore, the action of glutaminyl cyclase on DP IV inhibitors containing a homoglutaminyl residue, especially a L- $\alpha$ -homoglutaminyl residue at the N-terminus was unknown up to the present invention.

The ring closure reaction from the open chain glutaminy derivative being active as a DP IV inhibitor to the cyclic pyroglutaminy derivative (see scheme 1), which is inactive as a DP IV inhibitor *in vivo*, is accomplished by the enzyme glutaminy cyclase (hereinafter abbreviated as QC; E.C. 2.3.2.5) according to the reaction equation mentioned above.

Thus, the third object of the invention is solved by administration of an inhibitor for glutaminy cyclase (hereinafter abbreviated as QC inhibitor), which prevents the inactivation of the DP IV inhibitor molecule according to the present invention by cyclisation of their glutaminy or homoglutaminy residue, respectively. The administration of a glutaminy cyclase inhibitor in combination with a DP IV inhibitor according to the present invention containing a N-terminal glutaminy or homoglutaminy residue, respectively, therefore opens an additional option to control or to prolongate the half life period of the simultaneously administrated DP IV inhibitor, respectively. Therefore a definite and precise adjustment of the half life period of the DP IV inhibitors is possible according to the present invention by a simultaneous administration of both a QC and a DP IV inhibitor.

The DP IV inhibitor according to the present invention, optionally combined with a QC inhibitor, may then act within a definite time period as a medicament for the treatment of conditions mediated by DP IV or DP IV – like enzymes, such as arthritis, obesity, immune and autoimmune disorders, allograft transplantation, cancer, neuronal disorders and dermal diseases. Especially, the DP IV inhibitor according to the present invention, optionally combined with a QC inhibitor, may be used as a medicament for the treatment to improve glucose tolerance by lowering elevated blood glucose levels in response to an oral glucose challenge and, therefore, are useful in treating non-insulin dependent diabetes mellitus (NIDDM; DM Type 2).

Additionally, a synergistic action of DP IV inhibitors together with other proteins, which are cleaved and inactivated by DP IV, can be achieved by providing these proteins by a gene therapeutic expression systems in combination with the administration of DP IV inhibitors according to the present invention. These proteins

or peptides, respectively, are the glucagon like peptide 1 (GLP-1) and the glucose dependent insulintropic peptide (GIP) (see WO 03/030946).

Glucagon like peptide 1 (GLP-1) is a peptide synthesized in intestinal L cells in response to nutrient ingestion and promotes nutrient assimilation via potentiation of glucose dependent insulin secretion. Glucagon like peptide 1 (GLP-1) is produced by proteolytic cleavage of the proglucagon molecule. Functions of GLP-1 include the enhancement of regulated secretion of insulin from pancreatic  $\beta$ -cells in response to increased blood glucose levels and suppression of glucagon secretion, which together results in a decrease in blood glucose levels without causing hypoglycemia.

Glucagon like peptide 1 (GLP-1) has an extremely short half-life in vivo (< 2 minutes). In man, glucagon like peptide 1 (GLP-1), which has an alanine residue at position 2 is quickly inactivated by DP IV, which cleaves specifically dipeptides from peptides and proteins having an alanine or proline residue at position 2. Therefore, it is a further possibility for the treatment of type-2- diabetes and other DP IV related disorders, to provide glucagon like peptide 1 (GLP-1) by a gene therapeutic expression system on one hand, and to prevent the degradation of glucagon like peptide 1 (GLP-1) by DP IV on the other hand by simultaneous administration of DP IV inhibitors according to the present invention. By administering both GLP-1 and DP IV inhibitors, the half-life of GLP-1 is increased resulting in normalization of blood glucose levels in diabetic patients.

Further, glucose dependent insulintropic peptide (GIP), a peptide synthesized by duodenum K cells, functions to stimulate insulin release in response to increased blood glucose levels and may also have the advantage of lowering blood lipid levels. Glucose dependent insulintropic peptide (GIP) directly enhances insulin secretion through a specific GIP receptor expressed on islet  $\beta$ -cells. Unlike GLP-1, GIP has not been demonstrated to improve the phenotype of diabetic patients, although GIP has been shown to enhance insulin-mediated glucose disposal in sheep, rats and mice.

A recent study has demonstrated that, in a similar way to GLP-1, GIP is also inactivated through cleavage at position 2 alanine by DP IV. It has been found, that inhibition of DP IV reduces GIP degradation and potentiates its insulinotropic and antihyperglycemic effects in pigs. Therefore, the expression of GIP in the human body by a gene therapeutic expression system on one side, and the simultaneous administration of a DP IV inhibitor according to the present invention on the other side, is a further possibility to treat diabetes type 2 and DP IV related disorders.

Additionally, the coexpression of both GIP and GLP-1 by a gene therapeutic expression system on one side, and the simultaneous administration of DP IV inhibitors according to the present invention on the other side; represents a further option for an improved therapy for diabetes type 2 and DP IV related disorders, based on the fact, that the half-life of both GIP and GLP-1 is prolonged by simultaneous administration of DP IV inhibitors according to the present invention. Moreover, all therapies involving a gene therapeutic step may additionally be combined with the administration of a glutaminy cyclase inhibitor.

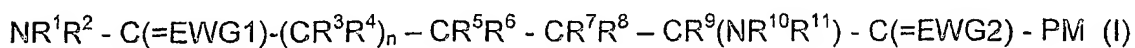
#### **Detailed description of the invention**

The present invention relates to the area of dipeptidyl peptidase IV (DPIV) inhibition and, more particularly, relates to glutaminy and homoglutaminy derivatives, wherein a glutaminy or homoglutaminy residue, respectively, is bound in a peptid manner to a nitrogen containing residue, pharmaceutical compositions containing said compounds, and the use of said compounds in inhibiting DPIV and DPIV-like enzyme activity.

The present invention provides new DPIV inhibitors, which are effective e.g. in treating conditions mediated by DPIV inhibition, pharmaceutical compositions e.g. useful in inhibiting DPIV and DPIV-like enzyme activity and a method of inhibiting DPIV and DPIV-like enzyme activity.

### Best embodiments for carrying out the invention

As a first embodiment, the present invention provides a compound of the formula



wherein  $n$  is 0 or 1;

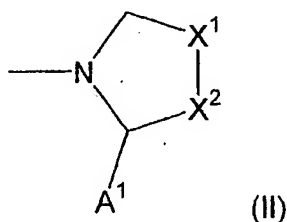
wherein  $\text{R}^1, \text{R}^2, \text{R}^3, \text{R}^4, \text{R}^5, \text{R}^6, \text{R}^7, \text{R}^8, \text{R}^9, \text{R}^{10}$ , and  $\text{R}^{11}$ , independently of each other, are

- a **hydrogen atom** (-H), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group or, a **carbaldehyde** (-CHO), a **ketone** group (-CO-R<sup>20</sup>), a **boronic acid** group (-B(OH)<sub>2</sub>), a **cyano** group (-C≡N), a **carboxylic acid** group (-COOH), a **carboxylic acid ester** group (-COOR<sup>21</sup>), a **carboxylic acid anhydride** group (-CO-O-CO-R<sup>22</sup>), a **hydroxamic acid** group (-CO-NH(OH)), a **N-substituted hydroxamic acid** group (-CO-NR<sup>23</sup>(OH)), a **O-substituted hydroxamic acid** group (-CO-NH(OR<sup>24</sup>)), a **carboxamide** group (-CO-NH<sub>2</sub>), a **N-substituted or N,N-disubstituted carboxylic acid amide** group, (-CO-NHR<sup>25</sup>; -CO-NR<sup>26</sup>R<sup>27</sup>), an **amido** group (-HN-CO-R<sup>28</sup>), a **sulfonic acid** group (-SO<sub>3</sub>H), a **sulfonamide** group (-SO<sub>2</sub>-NH<sub>2</sub>), a **N-substituted or N,N-disubstituted sulfonamide** group (-SO<sub>2</sub>-NHR<sup>29</sup>; -SO<sub>2</sub>-NR<sup>30</sup>R<sup>31</sup>), an **amidosulfone** group (-NH-SO<sub>2</sub>-R<sup>32</sup>), a **sulfone** group (-SO<sub>2</sub>-R<sup>33</sup>), a **phosphoric acid** group (-OP(=O)(OH)<sub>2</sub>), a **phosphoric acid ester** group (-OP(=O)(OR<sup>34</sup>)(OR<sup>35</sup>)), a **phosphonic acid** group (-P(=O)(OH)<sub>2</sub>), an **phosphonic acid ester** group (-P(=O)(OR<sup>36</sup>)(OR<sup>37</sup>)), a **halogen atom**, a **trifluormethyl** group (-CF<sub>3</sub>), a **thiol** group (-SH); a **thioether** group (-S-R<sup>38</sup>), a **hydroxy** group (-OH); an **alkoxy** group (-O-R<sup>39</sup>), a **tetrazole** group, an **amino** group (-NH<sub>2</sub>), or a **N-substituted or N,N-disubstituted amino** group (-NHR<sup>40</sup>; -NR<sup>41</sup>R<sup>42</sup>);
- which each independently can be **substituted** with one or more substituents, which can be the same or different; **and**,

- wherein optionally, any **two of the groups**  $R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}$ , and  $R^{11}$ , as well the pairs  $R^{26}/R^{27}, R^{30}/R^{31}, R^{34}/R^{35}, R^{36}/R^{37}$  and  $R^{41}/R^{42}$ , independently of each other, may form a part of a ring; and
- wherein the substituents  $R^{20}, R^{21}, R^{22}, R^{23}, R^{24}, R^{25}, R^{26}, R^{27}, R^{28}, R^{29}, R^{30}, R^{31}, R^{32}, R^{33}, R^{34}, R^{35}, R^{36}, R^{37}, R^{38}, R^{39}, R^{40}, R^{41}$ , and  $R^{42}$  independently of each other are a **hydrogen atom (-H)**, or an **alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl** group; and
- wherein EWG1 and EWG2 are each independently an electron withdrawing group and;

wherein the group PM

has the formula (II)



- wherein  $X^1$  is  $CR^{51}R^{52}$ , O, S, SO, SO<sub>2</sub> or  $NR^{53}$ ; and
- wherein  $X^2$  is  $CR^{54}R^{55}$ , O, S, SO, SO<sub>2</sub>, or  $NR^{56}$ ; and

wherein  $R^{51}, R^{52}, R^{53}, R^{54}, R^{55}$ , and  $R^{56}$ , independently of each other, are

- a **hydrogen atom (-H)**; or an **alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl** group or, a **carbaldehyde (-CHO)**, a **ketone**

group ( $-\text{CO}-\text{R}^{60}$ ), a **boronic acid** group ( $-\text{B}(\text{OH})_2$ ), a **cyano** group ( $-\text{C}\equiv\text{N}$ ), a **carboxylic acid** group ( $-\text{COOH}$ ), a **carboxylic acid ester** group ( $-\text{COOR}^{61}$ ), a **carboxylic acid anhydride** group ( $-\text{CO}-\text{O}-\text{CO}-\text{R}^{62}$ ), a **hydroxamic acid** group ( $-\text{CO}-\text{NH}(\text{OH})$ ), a N-substituted **hydroxamic acid** group ( $-\text{CO}-\text{NR}^{63}(\text{OH})$ ), a O-substituted **hydroxamic acid** group ( $-\text{CO}-\text{NH}(\text{OR}^{64})$ ), a **carboxamide** group ( $-\text{CO}-\text{NH}_2$ ), a N-substituted or N,N-disubstituted **carboxylic acid amide** group, ( $-\text{CO}-\text{NHR}^{65}$ ;  $-\text{CO}-\text{NR}^{66}\text{R}^{67}$ ), an **amido group** ( $-\text{HN}-\text{CO}-\text{R}^{68}$ ), a **sulfonic acid** group ( $-\text{SO}_3\text{H}$ ), a **sulfonamide** group ( $-\text{SO}_2-\text{NH}_2$ ), a N-substituted or N,N-disubstituted **sulfonamide** group ( $-\text{SO}_2-\text{NHR}^{69}$ ;  $-\text{SO}_2-\text{NR}^{70}\text{R}^{71}$ ), an **amidosulfone** group ( $-\text{NH}-\text{SO}_2-\text{R}^{72}$ ), a **sulfone** group ( $-\text{SO}_2-\text{R}^{73}$ ), a **phosphoric acid** group ( $-\text{OP}(=\text{O})(\text{OH})_2$ ), a **phosphoric acid ester** group ( $-\text{OP}(=\text{O})(\text{OR}^{74})(\text{OR}^{75})$ ), a **phosphonic acid** group ( $-\text{P}(=\text{O})(\text{OH})_2$ ), an **phosphonic acid ester** group ( $-\text{P}(=\text{O})(\text{OR}^{76})(\text{OR}^{77})$ ), a **halogen atom**, a **trifluormethyl** group ( $-\text{CF}_3$ ), a **thiol** group ( $-\text{SH}$ ); a **thioether** group ( $-\text{S}-\text{R}^{78}$ ), a **hydroxy** group ( $-\text{OH}$ ); an **alkoxy** group ( $-\text{O}-\text{R}^{79}$ ), a **tetrazole** group, an **amino** group ( $-\text{NH}_2$ ), or a N-substituted or N,N-disubstituted **amino** group ( $-\text{NHR}^{80}$ ;  $-\text{NR}^{81}\text{R}^{82}$ ); and

- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; and,
- wherein optionally, any **two of the groups**  $\text{R}^{51}$ ,  $\text{R}^{52}$ ,  $\text{R}^{53}$ ,  $\text{R}^{54}$ ,  $\text{R}^{55}$ , and  $\text{R}^{56}$ , if present, as well as the pairs  $\text{R}^{66}/\text{R}^{67}$ ,  $\text{R}^{70}/\text{R}^{71}$ ,  $\text{R}^{74}/\text{R}^{75}$ ,  $\text{R}^{76}/\text{R}^{77}$  and  $\text{R}^{81}/\text{R}^{82}$ , independently of each other, may form a part of a **ring**; and
- wherein the substituents  $\text{R}^{60}$ ,  $\text{R}^{61}$ ,  $\text{R}^{62}$ ,  $\text{R}^{63}$ ,  $\text{R}^{64}$ ,  $\text{R}^{65}$ ,  $\text{R}^{66}$ ,  $\text{R}^{67}$ ,  $\text{R}^{68}$ ,  $\text{R}^{69}$ ,  $\text{R}^{70}$ ,  $\text{R}^{71}$ ,  $\text{R}^{72}$ ,  $\text{R}^{73}$ ,  $\text{R}^{74}$ ,  $\text{R}^{75}$ ,  $\text{R}^{76}$ ,  $\text{R}^{77}$ ,  $\text{R}^{78}$ ,  $\text{R}^{79}$ ,  $\text{R}^{80}$ ,  $\text{R}^{81}$ , and  $\text{R}^{82}$ , independently of each other are a **hydrogen atom** ( $-\text{H}$ ), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group; and

wherein  $A^1$  is

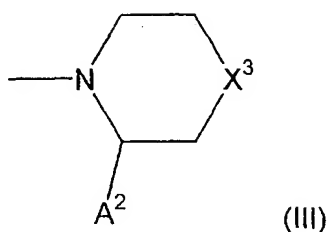
- a hydrogen atom (-H); or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group or, a carbaldehyde (-CHO), a ketone group ( $-\text{CO}-\text{R}^{100}$ ), a boronic acid group ( $-\text{B}(\text{OH})_2$ ), a cyano group ( $-\text{C}\equiv\text{N}$ ), a carboxylic acid group ( $-\text{COOH}$ ), a carboxylic acid ester group ( $-\text{COOR}^{101}$ ), a carboxylic acid anhydride group ( $-\text{CO}-\text{O}-\text{CO}-\text{R}^{102}$ ), a hydroxamic acid group ( $-\text{CO}-\text{NH}(\text{OH})$ ), a N-substituted hydroxamic acid group ( $-\text{CO}-\text{NR}^{103}(\text{OH})$ ), a O-substituted hydroxamic acid group ( $-\text{CO}-\text{NH}(\text{OR}^{104})$ ), a carboxamide group ( $-\text{CO}-\text{NH}_2$ ), a N-substituted or N,N-disubstituted carboxylic acid amide group, ( $-\text{CO}-\text{NHR}^{105}$ ;  $-\text{CO}-\text{NR}^{106}\text{R}^{107}$ ), an amido group ( $-\text{HN}-\text{CO}-\text{R}^{108}$ ), a sulfonic acid group ( $-\text{SO}_3\text{H}$ ), a sulfonamide group ( $-\text{SO}_2-\text{NH}_2$ ), a N-substituted or N,N-disubstituted sulfonamide group ( $-\text{SO}_2-\text{NHR}^{109}$ ;  $-\text{SO}_2-\text{NR}^{110}\text{R}^{111}$ ), an amidosulfone group ( $-\text{NH}-\text{SO}_2-\text{R}^{112}$ ), a sulfone group ( $-\text{SO}_2-\text{R}^{113}$ ), a phosphoric acid group ( $-\text{OP}(=\text{O})(\text{OH})_2$ ), a phosphoric acid ester group ( $-\text{OP}(=\text{O})(\text{OR}^{114})(\text{OR}^{115})$ ), a phosphonic acid group ( $-\text{P}(=\text{O})(\text{OH})_2$ ), an phosphonic acid ester group ( $-\text{P}(=\text{O})(\text{OR}^{116})(\text{OR}^{117})$ ), a halogen atom, a trifluormethyl group ( $-\text{CF}_3$ ), a thiol group ( $-\text{SH}$ ); a thioether group ( $-\text{S}-\text{R}^{118}$ ), a hydroxy group ( $-\text{OH}$ ); an alkoxy group ( $-\text{O}-\text{R}^{119}$ ), a tetrazole group, an amino group ( $-\text{NH}_2$ ), or a N-substituted or N,N-disubstituted amino group ( $-\text{NHR}^{120}$ ;  $-\text{NR}^{121}\text{R}^{122}$ ); and
- which, independently of each other, can be substituted with one or more substituents, which can be the same or different; and,
- wherein optionally, the pairs  $\text{R}^{106}/\text{R}^{107}$ ,  $\text{R}^{110}/\text{R}^{111}$ ,  $\text{R}^{114}/\text{R}^{115}$ ,  $\text{R}^{116}/\text{R}^{117}$  and  $\text{R}^{121}/\text{R}^{122}$ , independently of each other, may form a part of a ring; and
- wherein the substituents  $\text{R}^{100}$ ,  $\text{R}^{101}$ ,  $\text{R}^{102}$ ,  $\text{R}^{103}$ ,  $\text{R}^{104}$ ,  $\text{R}^{105}$ ,  $\text{R}^{106}$ ,  $\text{R}^{107}$ ,  $\text{R}^{108}$ ,  $\text{R}^{109}$ ,  $\text{R}^{110}$ ,  $\text{R}^{111}$ ,  $\text{R}^{112}$ ,  $\text{R}^{113}$ ,  $\text{R}^{114}$ ,  $\text{R}^{115}$ ,  $\text{R}^{116}$ ,  $\text{R}^{117}$ ,  $\text{R}^{118}$ ,  $\text{R}^{119}$ ,  $\text{R}^{120}$ ,  $\text{R}^{121}$ , and  $\text{R}^{122}$ , independently of each other are a hydrogen atom (-H), or an alkyl,



alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group;

or wherein the group PM

has the formula (III)



- wherein  $X^3$  is  $CR^{131}R^{132}$ , O, S, SO,  $SO_2$ , or  $NR^{133}$ ; and
- wherein  $R^{131}$ ,  $R^{132}$ , and  $R^{133}$ , independently of each other, are
- a hydrogen atom (-H); or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group or, a carbaldehyde (-CHO), a ketone group (-CO- $R^{140}$ ), a boronic acid group (-B(OH)<sub>2</sub>), a cyano group (-C≡N), a carboxylic acid group (-COOH), a carboxylic acid ester group (-COOR<sup>141</sup>), a carboxylic acid anhydride group (-CO-O-CO- $R^{142}$ ), a hydroxamic acid group (-CO-NH(OH)), a N-substituted hydroxamic acid group (-CO-NR<sup>143</sup>(OH)), a O-substituted hydroxamic acid group (-CO-NH(OR<sup>144</sup>)), a carboxamide group (-CO-NH<sub>2</sub>), a N-substituted or N,N-disubstituted carboxylic acid amide group, (-CO-NHR<sup>145</sup>; -CO-NR<sup>146</sup>R<sup>147</sup>), an amido group (-HN-CO- $R^{148}$ ), a sulfonic acid group (-SO<sub>3</sub>H), a sulfonamide group (-SO<sub>2</sub>-NH<sub>2</sub>), a N-substituted or N,N-disubstituted sulfonamide group (-SO<sub>2</sub>-NHR<sup>149</sup>; -SO<sub>2</sub>-NR<sup>150</sup>R<sup>151</sup>), an amidosulfone group (-NH-SO<sub>2</sub>- $R^{152}$ ), a sulfone group (-SO<sub>2</sub>- $R^{153}$ ), a phosphoric acid group (-OP(=O)(OH)<sub>2</sub>), a phosphoric acid ester group (-OP(=O)(OR<sup>154</sup>)(OR<sup>155</sup>)), a phosphonic acid group (-P(=O)(OH)<sub>2</sub>), an phosphonic acid ester group (-P(=O)(OR<sup>156</sup>)(OR<sup>157</sup>)), a halogen atom, a trifluormethyl group (-CF<sub>3</sub>), a thiol group (-SH); a thioether group (-S- $R^{158}$ ), a

hydroxy group (-OH); an alkoxy group (-O-R<sup>159</sup>), a tetrazole group, an amino group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted amino group (-NHR<sup>160</sup>; -NR<sup>161</sup>R<sup>162</sup>); and

- which, independently of each other, can be substituted with one or more substituents, which can be the same or different; and,
- wherein optionally, the the pair R<sup>131</sup>/R<sup>132</sup>, if present, as well the pairs R<sup>146</sup>/R<sup>147</sup>, R<sup>150</sup>/R<sup>151</sup>, R<sup>154</sup>/R<sup>155</sup>, R<sup>156</sup>/R<sup>157</sup> and R<sup>161</sup>/R<sup>162</sup>, independently of each other, may form a part of a ring; and
- wherein the substituents R<sup>140</sup>, R<sup>141</sup>, R<sup>142</sup>, R<sup>143</sup>, R<sup>144</sup>, R<sup>145</sup>, R<sup>146</sup>, R<sup>147</sup>, R<sup>148</sup>, R<sup>149</sup>, R<sup>150</sup>, R<sup>151</sup>, R<sup>152</sup>, R<sup>153</sup>, R<sup>154</sup>, R<sup>155</sup>, R<sup>156</sup>, R<sup>157</sup>, R<sup>158</sup>, R<sup>159</sup>, R<sup>160</sup>, R<sup>161</sup>, and R<sup>162</sup>, independently of each other are a hydrogen atom (-H), or an alkyl, alkenyl, alkinyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group;

wherein A<sup>2</sup> is

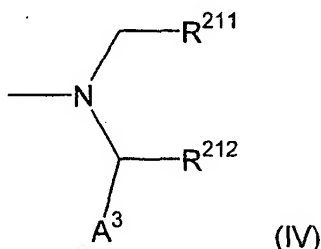
- a hydrogen atom (-H); or an alkyl, alkenyl, alkinyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group or, a carbaldehyde (-CHO), a ketone group (-CO-R<sup>180</sup>), a boronic acid group (-B(OH)<sub>2</sub>), a cyano group (-C≡N), a carboxylic acid group (-COOH), a carboxylic acid ester group (-COOR<sup>181</sup>), a carboxylic acid anhydride group (-CO-O-CO-R<sup>182</sup>), a hydroxamic acid group (-CO-NH(OH)), a N-substituted hydroxamic acid group (-CO-NR<sup>183</sup>(OH)), a O-substituted hydroxamic acid group (-CO-NH(OR<sup>184</sup>)), a carboxamide group (-CO-NH<sub>2</sub>), a N-substituted or N,N-disubstituted carboxylic acid amide group, (-CO-NHR<sup>185</sup>; -CO-NR<sup>186</sup>R<sup>187</sup>), an amido group (-HN-CO-R<sup>188</sup>), a sulfonic acid group (-SO<sub>3</sub>H), a sulfonamide group (-SO<sub>2</sub>-NH<sub>2</sub>), a N-substituted or N,N-disubstituted sulfonamide group (-SO<sub>2</sub>-NHR<sup>189</sup>; -SO<sub>2</sub>-NR<sup>190</sup>R<sup>191</sup>), an amidosulfone group (-NH-SO<sub>2</sub>-R<sup>192</sup>), a sulfone group (-SO<sub>2</sub>-R<sup>193</sup>), a phosphoric acid group (-OP(=O)(OH)<sub>2</sub>), a phosphoric acid ester group (-OP(=O)(OR<sup>194</sup>)(OR<sup>195</sup>)), a phosphonic acid group (-P(=O)(OH)<sub>2</sub>), an

phosphonic acid ester group ( $-P(=O)(OR^{196})(OR^{197})$ ), a halogen atom, a trifluormethyl group ( $-CF_3$ ), a thiol group ( $-SH$ ); a thioether group ( $-S-R^{198}$ ), a hydroxy group ( $-OH$ ); an alkoxy group ( $-O-R^{199}$ ), a tetrazole group, an amino group ( $-NH_2$ ), or a N-substituted or N,N-disubstituted amino group ( $-NHR^{200}$ ,  $-NR^{201}R^{202}$ ); and

- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the pairs  $R^{186}/R^{187}$ ,  $R^{190}/R^{191}$ ,  $R^{194}/R^{195}$ ,  $R^{196}/R^{197}$  and  $R^{201}/R^{202}$  independently of each other, may form a part of a ring; and
- wherein the substituents  $R^{180}$ ,  $R^{181}$ ,  $R^{182}$ ,  $R^{183}$ ,  $R^{184}$ ,  $R^{185}$ ,  $R^{186}$ ,  $R^{187}$ ,  $R^{188}$ ,  $R^{189}$ ,  $R^{190}$ ,  $R^{191}$ ,  $R^{192}$ ,  $R^{193}$ ,  $R^{194}$ ,  $R^{195}$ ,  $R^{196}$ ,  $R^{197}$ ,  $R^{198}$ ,  $R^{199}$ ,  $R^{200}$ ,  $R^{201}$ , and  $R^{202}$ , independently of each other are a **hydrogen atom** ( $-H$ ), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

or wherein the group **PM**

has the formula (IV)



- wherein  $R^{211}$  and  $R^{212}$ , independently of each other, are
- a **hydrogen atom** ( $-H$ ); or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group or, a **carbaldehyde** ( $-CHO$ ), a **ketone** group ( $-CO-R^{220}$ ), a **boronic acid** group ( $-B(OH)_2$ ), a **cyano** group ( $-C\equiv N$ ), a

carboxylic acid group (-COOH), a carboxylic acid ester group (-COOR<sup>221</sup>), a carboxylic acid anhydride group (-CO-O-CO-R<sup>222</sup>), a hydroxamic acid group (-CO-NH(OH)), a N-substituted hydroxamic acid group (-CO-NR<sup>223</sup>(OH)), a O-substituted hydroxamic acid group (-CO-NH(OR<sup>224</sup>)), a carboxamide group (-CO-NH<sub>2</sub>), a N-substituted or N,N-disubstituted carboxylic acid amide group, (-CO-NHR<sup>225</sup>; -CO-NR<sup>226</sup>R<sup>227</sup>), an amido group (-HN-CO-R<sup>228</sup>), a sulfonic acid group (-SO<sub>3</sub>H), a sulfonamide group (-SO<sub>2</sub>-NH<sub>2</sub>), a N-substituted or N,N-disubstituted sulfonamide group (-SO<sub>2</sub>-NHR<sup>229</sup>; -SO<sub>2</sub>-NR<sup>230</sup>R<sup>231</sup>), an amidosulfone group (-NH-SO<sub>2</sub>-R<sup>232</sup>), a sulfone group (-SO<sub>2</sub>-R<sup>233</sup>), a phosphoric acid group (-OP(=O)(OH)<sub>2</sub>), a phosphoric acid ester group (-OP(=O)(OR<sup>234</sup>)(OR<sup>235</sup>)), a phosphonic acid group (-P(=O)(OH)<sub>2</sub>), an phosphonic acid ester group (-P(=O)(OR<sup>236</sup>)(OR<sup>237</sup>)), a halogen atom, a trifluormethyl group (-CF<sub>3</sub>), a thiol group (-SH); a thioether group (-S-R<sup>238</sup>), a hydroxy group (-OH); an alkoxy group (-O-R<sup>239</sup>), a tetrazole group, an amino group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted amino group (-NHR<sup>240</sup>; -NR<sup>241</sup>R<sup>242</sup>); and

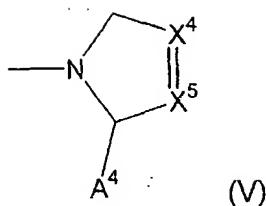
- which, independently of each other, can be substituted with one or more substituents, which can be the same or different; and,
- wherein optionally, the pairs R<sup>226</sup>/R<sup>227</sup>, R<sup>230</sup>/R<sup>231</sup>, R<sup>234</sup>/R<sup>235</sup>, R<sup>236</sup>/R<sup>237</sup> and R<sup>241</sup>/R<sup>242</sup>, independently of each other, may form a part of a ring; and
  - wherein the substituents R<sup>220</sup>, R<sup>221</sup>, R<sup>222</sup>, R<sup>223</sup>, R<sup>224</sup>, R<sup>225</sup>, R<sup>226</sup>, R<sup>227</sup>, R<sup>228</sup>, R<sup>229</sup>, R<sup>230</sup>, R<sup>231</sup>, R<sup>232</sup>, R<sup>233</sup>, R<sup>234</sup>, R<sup>235</sup>, R<sup>236</sup>, R<sup>237</sup>, R<sup>238</sup>, R<sup>239</sup>, R<sup>240</sup>, R<sup>241</sup>, and R<sup>242</sup>, independently of each other are a hydrogen atom (-H), or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group;
- wherein A<sup>3</sup> is
- a hydrogen atom (-H); or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group or, a carbaldehyde (-CHO), a ketone

- group ( $-\text{CO}-\text{R}^{260}$ ), a **boronic acid** group ( $-\text{B}(\text{OH})_2$ ), a **cyano** group ( $-\text{C}\equiv\text{N}$ ), a **carboxylic acid** group ( $-\text{COOH}$ ), a **carboxylic acid ester** group ( $-\text{COOR}^{261}$ ), a **carboxylic acid anhydride** group ( $-\text{CO}-\text{O}-\text{CO}-\text{R}^{262}$ ), a **hydroxamic acid** group ( $-\text{CO}-\text{NH}(\text{OH})$ ), a **N-substituted hydroxamic acid** group ( $-\text{CO}-\text{NR}^{263}(\text{OH})$ ), a **O-substituted hydroxamic acid** group ( $-\text{CO}-\text{NH}(\text{OR}^{264})$ ), a **carboxamide** group ( $-\text{CO}-\text{NH}_2$ ), a **N-substituted or N,N-disubstituted carboxylic acid amide** group, ( $-\text{CO}-\text{NHR}^{265}$ ;  $-\text{CO}-\text{NR}^{266}\text{R}^{267}$ ), an **amido** group ( $-\text{HN}-\text{CO}-\text{R}^{268}$ ), a **sulfonic acid** group ( $-\text{SO}_3\text{H}$ ), a **sulfonamide** group ( $-\text{SO}_2-\text{NH}_2$ ), a **N-substituted or N,N-disubstituted sulfonamide** group ( $-\text{SO}_2-\text{NHR}^{269}$ ;  $-\text{SO}_2-\text{NR}^{270}\text{R}^{271}$ ), an **amidosulfone** group ( $-\text{NH}-\text{SO}_2-\text{R}^{272}$ ), a **sulfone** group ( $-\text{SO}_2-\text{R}^{273}$ ), a **phosphoric acid** group ( $-\text{OP}(=\text{O})(\text{OH})_2$ ), a **phosphoric acid ester** group ( $-\text{OP}(=\text{O})(\text{OR}^{274})(\text{OR}^{275})$ ), a **phosphonic acid** group ( $-\text{P}(=\text{O})(\text{OH})_2$ ), an **phosphonic acid ester** group ( $-\text{P}(=\text{O})(\text{OR}^{276})(\text{OR}^{277})$ ), a **halogen atom**, a **trifluormethyl** group ( $-\text{CF}_3$ ), a **thiol** group ( $-\text{SH}$ ); a **thioether** group ( $-\text{S}-\text{R}^{278}$ ), a **hydroxy** group ( $-\text{OH}$ ); an **alkoxy** group ( $-\text{O}-\text{R}^{279}$ ), a **tetrazole** group, an **amino** group ( $-\text{NH}_2$ ), or a **N-substituted or N,N-disubstituted amino** group ( $-\text{NHR}^{280}$ ;  $-\text{NR}^{281}\text{R}^{282}$ ); and
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; and,
  - wherein optionally, the pairs  $\text{R}^{266}/\text{R}^{267}$ ,  $\text{R}^{270}/\text{R}^{271}$ ,  $\text{R}^{274}/\text{R}^{275}$ ,  $\text{R}^{276}/\text{R}^{277}$  and  $\text{R}^{281}/\text{R}^{282}$ , independently of each other, may form a part of a ring; and
  - wherein the substituents  $\text{R}^{260}$ ,  $\text{R}^{261}$ ,  $\text{R}^{262}$ ,  $\text{R}^{263}$ ,  $\text{R}^{264}$ ,  $\text{R}^{265}$ ,  $\text{R}^{266}$ ,  $\text{R}^{267}$ ,  $\text{R}^{268}$ ,  $\text{R}^{269}$ ,  $\text{R}^{270}$ ,  $\text{R}^{271}$ ,  $\text{R}^{272}$ ,  $\text{R}^{273}$ ,  $\text{R}^{274}$ ,  $\text{R}^{275}$ ,  $\text{R}^{276}$ ,  $\text{R}^{277}$ ,  $\text{R}^{278}$ ,  $\text{R}^{279}$ ,  $\text{R}^{280}$ ,  $\text{R}^{281}$ , and  $\text{R}^{282}$ , independently of each other are a **hydrogen atom** ( $-\text{H}$ ), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

or wherein the group PM

has the formula (V)

87



- wherein  $X^4$  is  $CR^{291}$  or N; and
- wherein  $X^5$  is  $CR^{292}$  or N; and
- wherein  $R^{291}$  and  $R^{292}$ , independently of each other, are
- a hydrogen atom (-H); or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group or, a carbaldehyde (-CHO), a ketone group (-CO- $R^{300}$ ), a boronic acid group (-B(OH)<sub>2</sub>), a cyano group (-C≡N), a carboxylic acid group (-COOH), a carboxylic acid ester group (-COOR<sup>301</sup>), a carboxylic acid anhydride group (-CO-O-CO- $R^{302}$ ), a hydroxamic acid group (-CO-NH(OH)), a N-substituted hydroxamic acid group (-CO-NR<sup>303</sup>(OH)), a O-substituted hydroxamic acid group (-CO-NH(OR<sup>304</sup>)), a carboxamide group (-CO-NH<sub>2</sub>), a N-substituted or N,N-disubstituted carboxylic acid amide group, (-CO-NHR<sup>305</sup>; -CO-NR<sup>306</sup>R<sup>307</sup>), an amido group (-HN-CO- $R^{308}$ ), a sulfonic acid group (-SO<sub>3</sub>H), a sulfonamide group (-SO<sub>2</sub>-NH<sub>2</sub>), a N-substituted or N,N-disubstituted sulfonamide group (-SO<sub>2</sub>-NHR<sup>309</sup>; -SO<sub>2</sub>-NR<sup>310</sup>R<sup>311</sup>), an amidosulfone group (-NH-SO<sub>2</sub>- $R^{312}$ ), a sulfone group (-SO<sub>2</sub>- $R^{313}$ ), a phosphoric acid group (-OP(=O)(OH)<sub>2</sub>), a phosphoric acid ester group (-OP(=O)(OR<sup>314</sup>)(OR<sup>315</sup>)), a phosphonic acid group (-P(=O)(OH)<sub>2</sub>), an phosphonic acid ester group (-P(=O)(OR<sup>316</sup>)(OR<sup>317</sup>)), a halogen atom, a trifluormethyl group (-CF<sub>3</sub>), a thiol group (-SH), a thioether group (-S- $R^{318}$ ), a hydroxy group (-OH); an alkoxy group (-O- $R^{319}$ ), a tetrazole group, an amino group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted amino group (-NHR<sup>320</sup>; -NR<sup>321</sup>R<sup>322</sup>); and

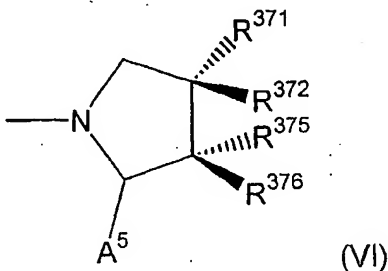
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the ~~the~~ pair  $R^{291}/R^{292}$ , if present, as well the pairs  $R^{306}/R^{307}$ ,  $R^{310}/R^{311}$ ,  $R^{314}/R^{315}$ ,  $R^{316}/R^{317}$  and  $R^{321}/R^{322}$ , independently of each other, may form a part of a **ring**; and
- wherein the substituents  $R^{300}$ ,  $R^{301}$ ,  $R^{302}$ ,  $R^{303}$ ,  $R^{304}$ ,  $R^{305}$ ,  $R^{306}$ ,  $R^{307}$ ,  $R^{308}$ ,  $R^{309}$ ,  $R^{310}$ ,  $R^{311}$ ,  $R^{312}$ ,  $R^{313}$ ,  $R^{314}$ ,  $R^{315}$ ,  $R^{316}$ ,  $R^{317}$ ,  $R^{318}$ ,  $R^{319}$ ,  $R^{320}$ ,  $R^{321}$ , and  $R^{322}$ , independently of each other are a **hydrogen atom (-H)**, or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;
- wherein  $A^4$  is
- a **hydrogen atom (-H)**; or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group or, a **carbaldehyde (-CHO)**, a **ketone group (-CO- $R^{340}$ )**, a **boronic acid group (-B(OH)<sub>2</sub>)**, a **cyano group (-C≡N)**, a **carboxylic acid group (-COOH)**, a **carboxylic acid ester group (-COOR<sup>341</sup>)**, a **carboxylic acid anhydride group (-CO-O-CO- $R^{342}$ )**, a **hydroxamic acid group (-CO-NH(OH))**, a **N-substituted hydroxamic acid group (-CO-NR<sup>343</sup>(OH))**, a **O-substituted hydroxamic acid group (-CO-NH(OR<sup>344</sup>))**, a **carboxamide group (-CO-NH<sub>2</sub>)**, a **N-substituted or N,N-disubstituted carboxylic acid amide group, (-CO-NHR<sup>345</sup>; -CO-NR<sup>346</sup> $R^{347}$ )**, an **amido group (-HN-CO- $R^{348}$ )**, a **sulfonic acid group (-SO<sub>3</sub>H)**, a **sulfonamide group (-SO<sub>2</sub>-NH<sub>2</sub>)**, a **N-substituted or N,N-disubstituted sulfonamide group (-SO<sub>2</sub>-NHR<sup>349</sup>; -SO<sub>2</sub>-NR<sup>350</sup> $R^{351}$ )**, an **amidosulfone group (-NH-SO<sub>2</sub>- $R^{352}$ )**, a **sulfone group (-SO<sub>2</sub>- $R^{353}$ )**, a **phosphoric acid group (-OP(=O)(OH)<sub>2</sub>)**, a **phosphoric acid ester group (-OP(=O)(OR<sup>354</sup>)(OR<sup>355</sup>))**, a **phosphonic acid group (-P(=O)(OH)<sub>2</sub>)**, an

phosphonic acid ester group ( $-P(=O)(OR^{356})(OR^{357})$ ), a halogen atom, a trifluormethyl group ( $-CF_3$ ), a thiol group ( $-SH$ ); a thioether group ( $-S-R^{358}$ ), a hydroxy group ( $-OH$ ); an alkoxy group ( $-O-R^{359}$ ), a tetrazole group, an amino group ( $-NH_2$ ), or a N-substituted or N,N-disubstituted amino group ( $-NHR^{360}$ ;  $-NR^{361}R^{362}$ ); and

- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the pairs  $R^{346}/R^{347}$ ,  $R^{350}/R^{351}$ ,  $R^{354}/R^{355}$ ,  $R^{356}/R^{357}$  and  $R^{361}/R^{362}$ , independently of each other, may form a part of a **ring**; and
- wherein the substituents  $R^{340}$ ,  $R^{341}$ ,  $R^{342}$ ,  $R^{343}$ ,  $R^{344}$ ,  $R^{345}$ ,  $R^{346}$ ,  $R^{347}$ ,  $R^{348}$ ,  $R^{349}$ ,  $R^{350}$ ,  $R^{351}$ ,  $R^{352}$ ,  $R^{353}$ ,  $R^{354}$ ,  $R^{355}$ ,  $R^{356}$ ,  $R^{357}$ ,  $R^{358}$ ,  $R^{359}$ ,  $R^{360}$ ,  $R^{361}$ , and  $R^{362}$ , independently of each other are a **hydrogen atom** ( $-H$ ), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

or wherein the group **PM**

has the formula (VI)



- wherein  $R^{371}$ ,  $R^{372}$ ,  $R^{375}$  and  $R^{376}$ , independently of each other,



a hydrogen atom (-H); or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group or, a carbaldehyde (-CHO), a ketone group ( $-\text{CO}-\text{R}^{380}$ ), a boronic acid group ( $-\text{B}(\text{OH})_2$ ), a cyano group ( $-\text{C}\equiv\text{N}$ ), a carboxylic acid group ( $-\text{COOH}$ ), a carboxylic acid ester group ( $-\text{COOR}^{381}$ ), a carboxylic acid anhydride group ( $-\text{CO}-\text{O}-\text{CO}-\text{R}^{382}$ ), a hydroxamic acid group ( $-\text{CO}-\text{NH}(\text{OH})$ ), a N-substituted hydroxamic acid group ( $-\text{CO}-\text{NR}^{383}(\text{OH})$ ), a O-substituted hydroxamic acid group ( $-\text{CO}-\text{NH}(\text{OR}^{384})$ ), a carboxamide group ( $-\text{CO}-\text{NH}_2$ ), a N-substituted or N,N-disubstituted carboxylic acid amide group, ( $-\text{CO}-\text{NHR}^{385}$ ;  $-\text{CO}-\text{NR}^{386}\text{R}^{387}$ ), an amido group ( $-\text{HN}-\text{CO}-\text{R}^{388}$ ), a sulfonic acid group ( $-\text{SO}_3\text{H}$ ), a sulfonamide group ( $-\text{SO}_2-\text{NH}_2$ ), a N-substituted or N,N-disubstituted sulfonamide group ( $-\text{SO}_2-\text{NHR}^{389}$ ;  $-\text{SO}_2-\text{NR}^{390}\text{R}^{391}$ ), an amidosulfone group ( $-\text{NH}-\text{SO}_2-\text{R}^{392}$ ), a sulfone group ( $-\text{SO}_2-\text{R}^{393}$ ), a phosphoric acid group ( $-\text{OP}(=\text{O})(\text{OH})_2$ ), a phosphoric acid ester group ( $-\text{OP}(=\text{O})(\text{OR}^{394})(\text{OR}^{395})$ ), a phosphonic acid group ( $-\text{P}(=\text{O})(\text{OH})_2$ ), an phosphonic acid ester group ( $-\text{P}(=\text{O})(\text{OR}^{396})(\text{OR}^{397})$ ), a halogen atom, a trifluormethyl group ( $-\text{CF}_3$ ), a thiol group ( $-\text{SH}$ ); a thioether group ( $-\text{S}-\text{R}^{398}$ ), a hydroxy group ( $-\text{OH}$ ); an alkoxy group ( $-\text{O}-\text{R}^{399}$ ), a tetrazole group, an amino group ( $-\text{NH}_2$ ), or a N-substituted or N,N-disubstituted amino group ( $-\text{NHR}^{400}$ ;  $-\text{NR}^{401}\text{R}^{402}$ ); and

- which, independently of each other, can be substituted with one or more substituents, which can be the same or different; and,
- wherein optionally, any two of the groups  $\text{R}^{371}$ ,  $\text{R}^{372}$ ,  $\text{R}^{375}$ , and  $\text{R}^{376}$ , as well as the pairs  $\text{R}^{386}/\text{R}^{387}$ ,  $\text{R}^{390}/\text{R}^{391}$ ,  $\text{R}^{394}/\text{R}^{395}$ ,  $\text{R}^{396}/\text{R}^{397}$  and  $\text{R}^{401}/\text{R}^{402}$ , independently of each other, may form a part of a ring; and
- wherein the substituents  $\text{R}^{380}$ ,  $\text{R}^{381}$ ,  $\text{R}^{382}$ ,  $\text{R}^{383}$ ,  $\text{R}^{384}$ ,  $\text{R}^{385}$ ,  $\text{R}^{386}$ ,  $\text{R}^{387}$ ,  $\text{R}^{388}$ ,  $\text{R}^{389}$ ,  $\text{R}^{390}$ ,  $\text{R}^{391}$ ,  $\text{R}^{392}$ ,  $\text{R}^{393}$ ,  $\text{R}^{394}$ ,  $\text{R}^{395}$ ,  $\text{R}^{396}$ ,  $\text{R}^{397}$ ,  $\text{R}^{398}$ ,  $\text{R}^{399}$ ,  $\text{R}^{400}$ ,  $\text{R}^{401}$ , and  $\text{R}^{402}$ , independently of each other are a hydrogen atom (-H), or an alkyl,

alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group; or

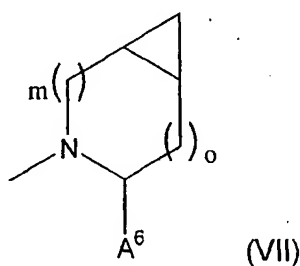
- alternatively; the two groups  $R^{371}$  and  $R^{372}$  can be together an **oxo** ( $=O$ ) or **hydroxyimino** ( $=N-OH$ ) group; and
- alternatively; the two groups  $R^{375}$  and  $R^{376}$  can be together an **oxo** ( $=O$ ) or **hydroxyimino** ( $=N-OH$ ) group; and
- 
- wherein  $A^5$  is
- a **hydrogen atom** ( $-H$ ); or an **alkyl**, **alkenyl**, **alkynyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group or, a **carbaldehyde** ( $-CHO$ ), a **ketone** group ( $-CO-R^{420}$ ), a **boronic acid** group ( $-B(OH)_2$ ), a **cyano** group ( $-C\equiv N$ ), a **carboxylic acid** group ( $-COOH$ ), a **carboxylic acid ester** group ( $-COOR^{421}$ ), a **carboxylic acid anhydride** group ( $-CO-O-CO-R^{422}$ ), a **hydroxamic acid** group ( $-CO-NH(OH)$ ), a **N-substituted hydroxamic acid** group ( $-CO-NR^{423}(OH)$ ), a **O-substituted hydroxamic acid** group ( $-CO-NH(OR^{424})$ ), a **carboxamide** group ( $-CO-NH_2$ ), a **N-substituted** or **N,N-disubstituted carboxylic acid amide** group, ( $-CO-NHR^{425}$ ;  $-CO-NR^{426}R^{427}$ ), an **amido** group ( $-HN-CO-R^{428}$ ), a **sulfonic acid** group ( $-SO_3H$ ), a **sulfonamide** group ( $-SO_2-NH_2$ ), a **N-substituted** or **N,N-disubstituted sulfonamide** group ( $-SO_2-NHR^{429}$ ;  $-SO_2-NR^{430}R^{431}$ ), an **amidosulfone** group ( $-NH-SO_2-R^{432}$ ), a **sulfone** group ( $-SO_2-R^{433}$ ), a **phosphoric acid** group ( $-OP(=O)(OH)_2$ ), a **phosphoric acid ester** group ( $-OP(=O)(OR^{434})(OR^{435})$ ), a **phosphonic acid** group ( $-P(=O)(OH)_2$ ), an **phosphonic acid ester** group ( $-P(=O)(OR^{436})(OR^{437})$ ), a **halogen atom**, a **trifluormethyl** group ( $-CF_3$ ), a **thiol** group ( $-SH$ ); a **thioether** group ( $-S-R^{438}$ ), a **hydroxy** group ( $-OH$ ); an **alkoxy** group ( $-O-R^{439}$ ), a **tetrazole** group, an **amino**

group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted **amino** group (-NHR<sup>440</sup>; -NR<sup>441</sup>R<sup>442</sup>); and

- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; and,
- wherein optionally, the pairs R<sup>426</sup>/R<sup>427</sup>, R<sup>430</sup>/R<sup>431</sup>, R<sup>434</sup>/R<sup>435</sup>, R<sup>436</sup>/R<sup>437</sup> and R<sup>441</sup>/R<sup>442</sup>, independently of each other, may form a part of a **ring**; and
- wherein the substituents R<sup>420</sup>, R<sup>421</sup>, R<sup>422</sup>, R<sup>423</sup>, R<sup>424</sup>, R<sup>425</sup>, R<sup>426</sup>, R<sup>427</sup>, R<sup>428</sup>, R<sup>429</sup>, R<sup>430</sup>, R<sup>431</sup>, R<sup>432</sup>, R<sup>433</sup>, R<sup>434</sup>, R<sup>435</sup>, R<sup>436</sup>, R<sup>437</sup>, R<sup>438</sup>, R<sup>439</sup>, R<sup>440</sup>, R<sup>441</sup>, and R<sup>442</sup>, independently of each other are a **hydrogen** atom (-H), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

or wherein the group **PM**

has the formula (VII)



- wherein m is equal to 1 or 2, and o is equal to 1 or 2, and m or o can be 0;
- wherein A<sup>6</sup> is a **hydrogen** atom (-H); or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**,

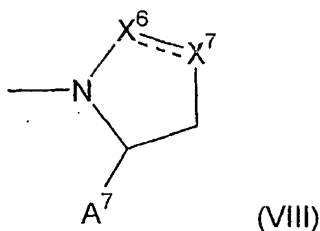
heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group or, a carbaldehyde (-CHO), a ketone group (-CO-R<sup>460</sup>), a boronic acid group (-B(OH)<sub>2</sub>), a cyano group (-C≡N), a carboxylic acid group (-COOH), a carboxylic acid ester group (-COOR<sup>461</sup>), a carboxylic acid anhydride group (-CO-O-CO-R<sup>462</sup>), a hydroxamic acid group (-CO-NH(OH)), a N-substituted hydroxamic acid group (-CO-NR<sup>463</sup>(OH)), a O-substituted hydroxamic acid group (-CO-NH(OR<sup>464</sup>)), a carboxamide group (-CO-NH<sub>2</sub>), a N-substituted or N,N-disubstituted carboxylic acid amide group, (-CO-NHR<sup>465</sup>; -CO-NR<sup>466</sup>R<sup>467</sup>), an amido group (-HN-CO-R<sup>468</sup>), a sulfonic acid group (-SO<sub>3</sub>H), a sulfonamide group (-SO<sub>2</sub>-NH<sub>2</sub>), a N-substituted or N,N-disubstituted sulfonamide group (-SO<sub>2</sub>-NHR<sup>469</sup>; -SO<sub>2</sub>-NR<sup>470</sup>R<sup>471</sup>), an amidosulfone group (-NH-SO<sub>2</sub>-R<sup>472</sup>), a sulfone group (-SO<sub>2</sub>-R<sup>473</sup>), a phosphoric acid group (-OP(=O)(OH)<sub>2</sub>), a phosphoric acid ester group (-OP(=O)(OR<sup>474</sup>)(OR<sup>475</sup>)), a phosphonic acid group (-P(=O)(OH)<sub>2</sub>), an phosphonic acid ester group (-P(=O)(OR<sup>476</sup>)(OR<sup>477</sup>)), a halogen atom, a trifluormethyl group (-CF<sub>3</sub>), a thiol group (-SH); a thioether group (-S-R<sup>478</sup>), a hydroxy group (-OH); an alkoxy group (-O-R<sup>479</sup>), a tetrazole group, an amino group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted amino group (-NHR<sup>480</sup>; -NR<sup>481</sup>R<sup>482</sup>);

- which, independently of each other, can be substituted with one or more substituents, which can be the same or different; and,
- wherein optionally, the pairs R<sup>466</sup>/R<sup>467</sup>, R<sup>470</sup>/R<sup>471</sup>, R<sup>474</sup>/R<sup>475</sup>, R<sup>476</sup>/R<sup>477</sup> and R<sup>481</sup>/R<sup>482</sup>, independently of each other, may form a part of a ring; and
- wherein the substituents R<sup>460</sup>, R<sup>461</sup>, R<sup>462</sup>, R<sup>463</sup>, R<sup>464</sup>, R<sup>465</sup>, R<sup>466</sup>, R<sup>467</sup>, R<sup>468</sup>, R<sup>469</sup>, R<sup>470</sup>, R<sup>471</sup>, R<sup>472</sup>, R<sup>473</sup>, R<sup>474</sup>, R<sup>475</sup>, R<sup>476</sup>, R<sup>477</sup>, R<sup>478</sup>, R<sup>479</sup>, R<sup>480</sup>, R<sup>481</sup>, and R<sup>482</sup>, independently of each other are a hydrogen atom (-H), or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl,

heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group;

or wherein the group PM

has the formula (VIII)



- wherein  $X^6$  is selected from  $CR^{490}R^{491}$ , O, S or  $NR^{492}$ , when the bond between  $X^6$  and  $X^7$  is a single bond; and
- wherein  $X^7$  is selected from  $CR^{493}R^{494}$ , O, S, or  $NR^{495}$ , when the bond between  $X^6$  and  $X^7$  is a single bond;
- **or alternatively,**
- wherein  $X^6$  is selected from  $CR^{496}$  or N, when the bond between  $X^6$  and  $X^7$  is a double bond; and
- wherein  $X^7$  is selected from  $CR^{497}$  or N, when the bond between  $X^6$  and  $X^7$  is a double bond; and
- wherein  $R^{490}$ ,  $R^{491}$ ,  $R^{492}$ ,  $R^{493}$ ,  $R^{494}$ ,  $R^{495}$ ,  $R^{496}$ , and  $R^{497}$ , independently of each other, are a **hydrogen atom (-H)**; or an **alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl** group or, a **carbaldehyde (-CHO)**, a **ketone group (-CO-R<sup>500</sup>)**, a **boronic acid group (-B(OH)<sub>2</sub>)**, a **cyano group (-C≡N)**, a **carboxylic acid group (-COOH)**, a **carboxylic acid ester group (-COOR<sup>501</sup>)**, a **carboxylic acid anhydride group (-CO-O-CO-R<sup>502</sup>)**, a

**hydroxamic acid** group (-CO-NH(OH)), a N-substituted **hydroxamic acid** group (-CO-NR<sup>503</sup>(OH)), a O-substituted **hydroxamic acid** group (-CO-NH(OR<sup>504</sup>)), a **carboxamide** group (-CO-NH<sub>2</sub>), a N-substituted or N,N-disubstituted **carboxylic acid amide** group, (-CO-NHR<sup>505</sup>; -CO-NR<sup>506</sup>R<sup>507</sup>), an **amido** group (-HN-CO-R<sup>508</sup>), a **sulfonic acid** group (-SO<sub>3</sub>H), a **sulfonamide** group (-SO<sub>2</sub>-NH<sub>2</sub>), a N-substituted or N,N-disubstituted **sulfonamide** group (-SO<sub>2</sub>-NHR<sup>509</sup>; -SO<sub>2</sub>-NR<sup>510</sup>R<sup>511</sup>), an **amidosulfone** group (-NH-SO<sub>2</sub>-R<sup>512</sup>), a **sulfone** group (-SO<sub>2</sub>-R<sup>513</sup>), a **phosphoric acid** group (-OP(=O)(OH)<sub>2</sub>), a **phosphoric acid ester** group (-OP(=O)(OR<sup>514</sup>)(OR<sup>515</sup>)), a **phosphonic acid** group (-P(=O)(OH)<sub>2</sub>), an **phosphonic acid ester** group (-P(=O)(OR<sup>516</sup>)(OR<sup>517</sup>)), a **halogen atom**, a **trifluormethyl** group (-CF<sub>3</sub>), a **thiol** group (-SH); a **thioether** group (-S-R<sup>518</sup>), a **hydroxy** group (-OH); an **alkoxy** group (-O-R<sup>519</sup>), a **tetrazole** group, an **amino** group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted **amino** group (-NHR<sup>520</sup>; -NR<sup>521</sup>R<sup>522</sup>); and

- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, any two the groups R<sup>490</sup>, R<sup>491</sup>, R<sup>492</sup>, R<sup>493</sup>, R<sup>494</sup>, R<sup>495</sup>, R<sup>496</sup>, and R<sup>497</sup>, if present, as well as the pairs R<sup>506</sup>/R<sup>507</sup>, R<sup>510</sup>/R<sup>511</sup>, R<sup>514</sup>/R<sup>515</sup>, R<sup>516</sup>/R<sup>517</sup> and R<sup>521</sup>/R<sup>522</sup>, independently of each other, may form a part of a **ring**; and
- wherein the substituents R<sup>500</sup>, R<sup>501</sup>, R<sup>502</sup>, R<sup>503</sup>, R<sup>504</sup>, R<sup>505</sup>, R<sup>506</sup>, R<sup>507</sup>, R<sup>508</sup>, R<sup>509</sup>, R<sup>510</sup>, R<sup>511</sup>, R<sup>512</sup>, R<sup>513</sup>, R<sup>514</sup>, R<sup>515</sup>, R<sup>516</sup>, R<sup>517</sup>, R<sup>518</sup>, R<sup>519</sup>, R<sup>520</sup>, R<sup>521</sup>, and R<sup>522</sup>, independently of each other are a **hydrogen atom** (-H), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group; and
- wherein A<sup>7</sup> is
- a **hydrogen atom** (-H); or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**,

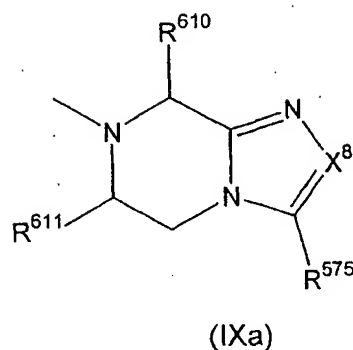
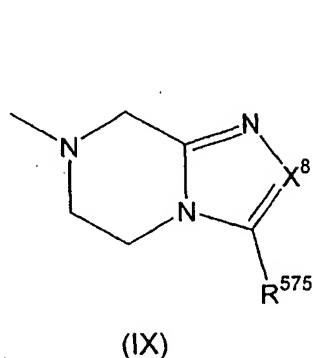
heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group or, a carbaldehyde (-CHO), a ketone group (-CO-R<sup>540</sup>), a boronic acid group (-B(OH)<sub>2</sub>), a cyano group (-C≡N), a carboxylic acid group (-COOH), a carboxylic acid ester group (-COOR<sup>541</sup>), a carboxylic acid anhydride group (-CO-O-CO-R<sup>542</sup>), a hydroxamic acid group (-CO-NH(OH)), a N-substituted hydroxamic acid group (-CO-NR<sup>543</sup>(OH)), a O-substituted hydroxamic acid group (-CO-NH(OR<sup>544</sup>)), a carboxamide group (-CO-NH<sub>2</sub>), a N-substituted or N,N-disubstituted carboxylic acid amide group, (-CO-NHR<sup>545</sup>; -CO-NR<sup>546</sup>R<sup>547</sup>), an amido group (-HN-CO-R<sup>548</sup>), a sulfonic acid group (-SO<sub>3</sub>H), a sulfonamide group (-SO<sub>2</sub>-NH<sub>2</sub>), a N-substituted or N,N-disubstituted sulfonamide group (-SO<sub>2</sub>-NHR<sup>549</sup>; -SO<sub>2</sub>-NR<sup>550</sup>R<sup>551</sup>), an amidosulfone group (-NH-SO<sub>2</sub>-R<sup>552</sup>), a sulfone group (-SO<sub>2</sub>-R<sup>553</sup>), a phosphoric acid group (-OP(=O)(OH)<sub>2</sub>), a phosphoric acid ester group (-OP(=O)(OR<sup>554</sup>)(OR<sup>555</sup>)), a phosphonic acid group (-P(=O)(OH)<sub>2</sub>), an phosphonic acid ester group (-P(=O)(OR<sup>556</sup>)(OR<sup>557</sup>)), a halogen atom, a trifluormethyl group (-CF<sub>3</sub>), a thiol group (-SH), a thioether group (-S-R<sup>558</sup>), a hydroxy group (-OH), an alkoxy group (-O-R<sup>559</sup>), a tetrazole group, an amino group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted amino group (-NHR<sup>560</sup>; -NR<sup>561</sup>R<sup>562</sup>); and

- which, independently of each other, can be substituted with one or more substituents, which can be the same or different; and,
- wherein optionally, the pairs R<sup>546</sup>/R<sup>547</sup>, R<sup>550</sup>/R<sup>551</sup>, R<sup>554</sup>/R<sup>555</sup>, R<sup>556</sup>/R<sup>557</sup> and R<sup>561</sup>/R<sup>562</sup>, independently of each other, may form a part of a ring; and
- wherein the substituents R<sup>540</sup>, R<sup>541</sup>, R<sup>542</sup>, R<sup>543</sup>, R<sup>544</sup>, R<sup>545</sup>, R<sup>546</sup>, R<sup>547</sup>, R<sup>548</sup>, R<sup>549</sup>, R<sup>550</sup>, R<sup>551</sup>, R<sup>552</sup>, R<sup>553</sup>, R<sup>554</sup>, R<sup>555</sup>, R<sup>556</sup>, R<sup>557</sup>, R<sup>558</sup>, R<sup>559</sup>, R<sup>560</sup>, R<sup>561</sup>, and R<sup>562</sup>, independently of each other are a hydrogen atom (-H), or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl,

heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group;

or wherein the group PM

has the formula (IX) or (IXa)



- wherein  $X^8$  is N or  $CR^{570}$ ; and
- wherein  $R^{570}$ ,  $R^{575}$ ,  $R^{610}$  and  $R^{611}$  independently of each other, are a hydrogen atom (-H); or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group or, a carbaldehyde (-CHO), a ketone group (-CO- $R^{580}$ ), a boronic acid group (-B(OH)<sub>2</sub>), a cyano group (-C≡N), a carboxylic acid group (-COOH), a carboxylic acid ester group (-COOR<sup>581</sup>), a carboxylic acid anhydride group (-CO-O-CO- $R^{582}$ ), a hydroxamic acid group (-CO-NH(OH)), a N-substituted hydroxamic acid group (-CO-NR<sup>583</sup>(OH)), a O-substituted hydroxamic acid group (-CO-NH(OR<sup>584</sup>)), a carboxamide group (-CO-NH<sub>2</sub>), a N-substituted or N,N-disubstituted carboxylic acid amide group, (-CO-NHR<sup>585</sup>; -CO-NR<sup>586</sup>R<sup>587</sup>), an amido group (-HN-CO- $R^{588}$ ), a sulfonic acid group (-SO<sub>3</sub>H), a sulfonamide group (-SO<sub>2</sub>-NH<sub>2</sub>), a N-substituted or N,N-disubstituted sulfonamide group (-SO<sub>2</sub>-NHR<sup>589</sup>; -SO<sub>2</sub>-NR<sup>590</sup>R<sup>591</sup>), an amidosulfone group (-NH-SO<sub>2</sub>- $R^{592}$ ), a sulfone group (-SO<sub>2</sub>-

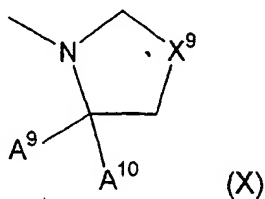


$R^{593}$ ), a **phosphoric acid** group ( $-\text{OP}(=\text{O})(\text{OH})_2$ ), a **phosphoric acid ester** group ( $-\text{OP}(=\text{O})(\text{OR}^{594})(\text{OR}^{595})$ ), a **phosphonic acid** group ( $-\text{P}(=\text{O})(\text{OH})_2$ ), an **phosphonic acid ester** group ( $-\text{P}(=\text{O})(\text{OR}^{596})(\text{OR}^{597})$ ), a **halogen atom**, a **trifluormethyl** group ( $-\text{CF}_3$ ), a **thiol** group ( $-\text{SH}$ ); a **thioether** group ( $-\text{S}-\text{R}^{598}$ ), a **hydroxy** group ( $-\text{OH}$ ); an **alkoxy** group ( $-\text{O}-\text{R}^{599}$ ), a **tetrazole** group, an **amino** group ( $-\text{NH}_2$ ), or a **N-substituted** or **N,N-disubstituted amino** group ( $-\text{NHR}^{600}$ ;  $-\text{NR}^{601}\text{R}^{602}$ );

- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the pairs  $\text{R}^{570}/\text{R}^{575}$ , if present, as well as the pairs  $\text{R}^{586}/\text{R}^{587}$ ,  $\text{R}^{590}/\text{R}^{591}$ ,  $\text{R}^{594}/\text{R}^{595}$ ,  $\text{R}^{596}/\text{R}^{597}$  and  $\text{R}^{601}/\text{R}^{602}$ , independently of each other, may form a part of a **ring**; and
- wherein the substituents  $\text{R}^{580}$ ,  $\text{R}^{581}$ ,  $\text{R}^{582}$ ,  $\text{R}^{583}$ ,  $\text{R}^{584}$ ,  $\text{R}^{585}$ ,  $\text{R}^{586}$ ,  $\text{R}^{587}$ ,  $\text{R}^{588}$ ,  $\text{R}^{589}$ ,  $\text{R}^{590}$ ,  $\text{R}^{591}$ ,  $\text{R}^{592}$ ,  $\text{R}^{593}$ ,  $\text{R}^{594}$ ,  $\text{R}^{595}$ ,  $\text{R}^{596}$ ,  $\text{R}^{597}$ ,  $\text{R}^{598}$ ,  $\text{R}^{599}$ ,  $\text{R}^{600}$ ,  $\text{R}^{601}$ , and  $\text{R}^{602}$ , independently of each other are a **hydrogen atom** ( $-\text{H}$ ), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

**or wherein the group PM**

has the formula (X)



- wherein the groups  $X^9$  is  $CR^{900}R^{901}$ , S, SO,  $SO_2$  or  $NR^{902}$ 
  - wherein  $R^{900}$ ,  $R^{901}$  and  $R^{902}$ , are, independently of each other, selected from hydrogen, fluorine,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens, or  $-C(=O)NR^{910}R^{911}$ .
- wherein  $A^9$  and  $A^{10}$  are, independently of each other, selected from hydrogen, cyano,  $-C(=O)NR^{912}R^{913}$ , or  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein

- $R^{910}$  and  $R^{912}$ , are, independently of each other, selected from hydrogen, or  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens; and
- $R^{911}$  and  $R^{913}$ , are, independently of each other, selected from the group consisting of

(1) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5, substituents independently selected from halogen and  $R^{920}$ ;

(2)  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6 or 7 substituents independently selected from (a) 0, 1, 2, 3, 4, or 5 halogens, and (b) 0, 1, 2 substituents selected from the group consisting of

- (a) hydroxy,
- (b)  $-COOH$ ,
- (c)  $-COO(C_1, C_2, C_3, C_4, C_5$  or  $C_6$  alkyl), i.e. ester,
- (d) phenyl,
- (e) naphthyl,
- (f)  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  cycloalkyl,
- (g) a 5 - or 6 membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur;
- (h) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (a) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected

from nitrogen, oxygen or sulfur, or (b) a benzene ring fused to a 5- or 6-membered heterocycle having 1, 2, or 3 hetero atoms;

- wherein said C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl, phenyl, naphthyl, are optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from halogen and R<sup>920</sup>, and said 5 or 6 membered heterocycle and said 8, 9 or 10 - membered bicyclic ring system are each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, and R<sup>920</sup>; and

(3) C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl, which is optionally substituted with 1, 2, or 3 groups independently selected from halogen, hydroxy, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein R<sup>920</sup> is selected from the group consisting of:

(1) hydroxy;

(2) cyano;

(3) C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl optionally substituted with 1, 2, or 3 groups independently selected from halogen, hydroxy, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, wherein said -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl are linear or branched and are optionally substituted with 1, 2, 3, 4, 5 or 6 substituents selected from 1, 2, 3, 4, or 5 halogens, and 0 or 1 substituents selected from -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, -COOH, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl substituents being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(4) C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub>, C<sub>9</sub> or C<sub>10</sub> alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6, or 7 substituents independently selected from 0, 1, 2, 3, 4, or 5 halogen atoms and 0, 1, or 2 groups selected from

(a) hydroxy;

(b) -COOH;

- (c)  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester, which may linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens;
- (d) a 5- or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen,  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5$  or  $-\text{OC}_6$  alkyl, said  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5$  or  $-\text{OC}_6$  alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.;
- (e) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (i) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (ii) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen,  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5$  or  $-\text{OC}_6$  alkyl, said  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5$  or  $-\text{OC}_6$  alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;
- (f)  $-\text{CONR}^{925}\text{R}^{925}$ ;
- (g)  $-\text{SO}_2\text{NR}^{925}\text{R}^{925}$ ;
- (h)  $-\text{NR}^{925}-\text{C}(=\text{O})\text{R}^{925}$ ;
- (i)  $-\text{NR}^{925}-\text{C}(=\text{O})\text{NR}^{925}\text{R}^{925}$ ;
- (j)  $-\text{NR}^{925}\text{COOR}^{930}$ ;
- (k)  $-\text{O}-\text{CO}-\text{R}^{930}$ ;
- (l)  $-\text{O}-\text{CO}-\text{NR}^{925}\text{R}^{925}$ ;
- (m)  $-\text{NR}^{925}\text{SO}_2\text{R}^{930}$ ;
- (n)  $-\text{NR}^{925}\text{R}^{925}$ ;
- (o) phenyl which is optionally substituted with 1, 2, 3, 4, or 5 group independently selected from halogen, hydroxy,  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  alkyl,  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5$  or  $-\text{OC}_6$  alkyl,  $-\text{COOH}$ ,  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester, said  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  alkyl,  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5$  or  $-\text{OC}_6$  alkyl,  $-\text{COOH}$ ,  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester being linear or branched and optionally substituted

with 1, 2, 3, 4, 5, or 6 substituents independently selected from 0 or 1

C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl and 0, 1, 2, 3, 4, or 5 halogens, and

(p) C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, which is optionally substituted with 1, 2, 3, 4, 5, or 6 halogens;

(5) OC<sub>1</sub>, OC<sub>2</sub>, OC<sub>3</sub>, OC<sub>4</sub>, OC<sub>5</sub>, OC<sub>6</sub>, OC<sub>7</sub>, OC<sub>8</sub>, OC<sub>9</sub> or OC<sub>10</sub> alkyl, which is linear or branched and is optionally substituted with 0, 1, 2, 3, 4, or 5 halogen atoms and 0, 1, or 2 substituents selected from

(a) hydroxy;

(b) -COOH;

(c) -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, which may be linear or branched and is optionally substituted with 1, 2, 3, 4 or 5 halogens;

(d) a 5- or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.;

(e) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (i) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (ii) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(f) -CONR<sup>925</sup>R<sup>925</sup>;

(g) -SO<sub>2</sub>NR<sup>925</sup>R<sup>925</sup>;

(h) -NR<sup>925</sup>-C(=O)R<sup>925</sup>

(i) -NR<sup>925</sup>-C(=O)NR<sup>925</sup>R<sup>925</sup>;

(j) -NR<sup>925</sup>COOR<sup>930</sup>

(k) -O-CO-R<sup>930</sup>

- (l)  $-O-CO-NR^{925}R^{925}$ ;
- (m)  $-NR^{925}SO_2R^{930}$ ;
- (n)  $-NR^{925}R^{925}$ ;
- (o) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5 groups independently selected from halogen, hydroxy,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl,  $-OC_1$ ,  $-OC_2$ ,  $-OC_3$ ,  $-OC_4$ ,  $-OC_5$  or  $-OC_6$  alkyl,  $-COOH$ ,  $-COO(C_1, C_2, C_3, C_4, C_5$  or  $C_6$  alkyl) i.e. ester, said  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl,  $-OC_1$ ,  $-OC_2$ ,  $-OC_3$ ,  $-OC_4$ ,  $-OC_5$  or  $-OC_6$  alkyl,  $-COOH$ ,  $-COO(C_1, C_2, C_3, C_4, C_5$  or  $C_6$  alkyl) i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, 5, or 6 substituents independently selected from 0 or 1  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  cycloalkyl and 0, 1, 2, 3, 4, or 5 halogens, and
- (p)  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  cycloalkyl, which is optionally substituted with 1, 2, 3, 4, 5, or 6 halogens;
- (6)  $-COOH$ ;
- (7)  $-COO(C_1, C_2, C_3, C_4, C_5$  or  $C_6$  alkyl) i.e. ester, which may be linear or branched and is optionally substituted with 1, 2, 3, 4, 5 halogens;
- (8) a 5- or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, said heterocycle being optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl, and  $-OC_1$ ,  $-OC_2$ ,  $-OC_3$ ,  $-OC_4$ ,  $-OC_5$  or  $-OC_6$  alkyl, said  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl, and  $-OC_1$ ,  $-OC_2$ ,  $-OC_3$ ,  $-OC_4$ ,  $-OC_5$  or  $-OC_6$  alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.
- (9) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (a) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (b) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl, and  $-OC_1$ ,  $-OC_2$ ,  $-OC_3$ ,  $-OC_4$ ,  $-OC_5$  or  $-OC_6$  alkyl, said  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl, and  $-OC_1$ ,  $-OC_2$ ,  $-OC_3$ ,  $-OC_4$ ,  $-OC_5$  or  $-OC_6$  alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;
- (10)  $-CONR^{925}R^{925}$ ;
- (11)  $-SO_2NR^{925}R^{925}$ ;

(12)  $-\text{NR}^{925}-\text{C}(=\text{O})\text{R}^{925}$

(13)  $-\text{NR}^{925}-\text{C}(=\text{O})\text{NR}^{925}\text{R}^{925}$ ;

(14)  $-\text{NR}^{925}\text{COOR}^{930}$

(15)  $-\text{O}-\text{CO}-\text{R}^{930}$

(16)  $-\text{O}-\text{CO}-\text{NR}^{925}\text{R}^{925}$ ;

(17)  $-\text{NR}^{925}\text{SO}_2\text{R}^{930}$ ;

(18)  $-\text{NR}^{925}\text{R}^{925}$ ;

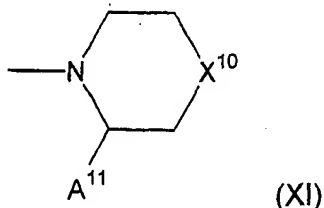
(19) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5 group independently selected from halogen, hydroxy,  $\text{C}_1$ ,  $\text{C}_2$ ,  $\text{C}_3$ ,  $\text{C}_4$ ,  $\text{C}_5$  or  $\text{C}_6$  alkyl,  $-\text{OC}_1$ ,  $-\text{OC}_2$ ,  $-\text{OC}_3$ ,  $-\text{OC}_4$ ,  $-\text{OC}_5$  or  $-\text{OC}_6$  alkyl,  $-\text{COOH}$ ,  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  alkyl) i.e. ester, said  $\text{C}_1$ ,  $\text{C}_2$ ,  $\text{C}_3$ ,  $\text{C}_4$ ,  $\text{C}_5$  or  $\text{C}_6$  alkyl,  $-\text{OC}_1$ ,  $-\text{OC}_2$ ,  $-\text{OC}_3$ ,  $-\text{OC}_4$ ,  $-\text{OC}_5$  or  $-\text{OC}_6$  alkyl,  $-\text{COOH}$ ,  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  alkyl) i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein  $\text{R}^{930}$  is selected from the group consisting of phenyl,  $\text{C}_3$ ,  $\text{C}_4$ ,  $\text{C}_5$  or  $\text{C}_6$  cycloalkyl, and  $\text{C}_3$ ,  $\text{C}_4$ ,  $\text{C}_5$  or  $\text{C}_6$  cycloalkyl, wherein  $\text{C}_1$ ,  $\text{C}_2$ ,  $\text{C}_3$ ,  $\text{C}_4$ ,  $\text{C}_5$  or  $\text{C}_6$  alkyl is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6, substituents independently selected from 0, 1, 2, 3, 4, or 5 halogens, 0 or 1 phenyl, wherein said optional phenyl substituent and said  $\text{R}^{930}$ , when  $\text{R}^{930}$  is phenyl or  $\text{C}_3$ ,  $\text{C}_4$ ,  $\text{C}_5$  or  $\text{C}_6$  cycloalkyl, are optionally substituted with 1, 2, 3, 4, or 5 substituents, independently selected from halogen, OH,  $\text{C}_1$ ,  $\text{C}_2$ ,  $\text{C}_3$ ,  $\text{C}_4$ , or  $\text{C}_5$  alkyl,  $-\text{OC}_1$ ,  $-\text{OC}_2$ ,  $-\text{OC}_3$ ,  $-\text{OC}_4$ , or  $-\text{OC}_5$  alkyl, said  $\text{C}_1$ ,  $\text{C}_2$ ,  $\text{C}_3$ ,  $\text{C}_4$ , or  $\text{C}_5$  alkyl,  $-\text{OC}_1$ ,  $-\text{OC}_2$ ,  $-\text{OC}_3$ ,  $-\text{OC}_4$ , or  $-\text{OC}_5$  alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.

wherein  $\text{R}^{925}$  is selected from  $\text{R}^{930}$  and hydrogen.

wherein the group PM

has the formula (XI)



- wherein the groups  $X^{10}$  is  $CR^{1000}R^{1001}$ , S, SO,  $SO_2$  or  $NR^{1002}$
- wherein  $R^{1000}$ ,  $R^{1001}$  and  $R^{1002}$ , are, independently of each other, selected from hydrogen, fluorine,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens, or  $-C(=O)NR^{910}R^{911}$ .

and  $A^{11}$  is selected from

hydrogen, cyano,  $-C(=O)NR^{1012}R^{1013}$ , or  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein

- $R^{1010}$  and  $R^{1012}$ , are, independently of each other, selected from hydrogen, or  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens; and
- $R^{1011}$  and  $R^{1013}$ , are, independently of each other, selected from the group consisting of

(1) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5, substituents independently selected from halogen and  $R^{1020}$ ;

(2)  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6 or 7 substituents independently selected from (a) 0, 1, 2, 3, 4, or 5 halogens, and (b) 0, 1, 2 substituents selected from the group consisting of

- (a) hydroxy,
- (b)  $-COOH$ ,
- (c)  $-COO(C_1, C_2, C_3, C_4, C_5 \text{ or } C_6 \text{ alkyl})$ , i.e. ester,
- (d) phenyl,
- (e) naphthyl,
- (f)  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  cycloalkyl,
- (g) a 5 - or 6 membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur;
- (h) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (a) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected



from nitrogen, oxygen or sulfur, or (b) a benzene ring fused to a 5- or 6-membered heterocycle having 1, 2, or 3 hetero atoms;

- wherein said C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl, phenyl, naphthyl, are optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from halogen and R<sup>1020</sup>, and said 5 or 6 membered heterocycle and said 8, 9 or 10 - membered bicyclic ring system are each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from from oxo, hydroxy, halogen, and R<sup>1020</sup>; and

(3) C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl, which is optionally substituted with 1, 2, or 3 groups independently selected from halogen, hydroxy, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein R<sup>1020</sup> is selected from the group consisting of:

(1) hydroxy;

(2) cyano;

(3) C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl optionally substituted with 1, 2, or 3 groups independently selected from halogen, hydroxy, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, wherein said -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl are linear or branched and are optionally substituted with 1, 2, 3, 4, 5 or 6 substituents selected from 1, 2, 3, 4, or 5 halogens, and 0 or 1 substituents selected from -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, -COOH, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl substituents being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(4) C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub>, C<sub>9</sub> or C<sub>10</sub> alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6, or 7 substituents independently selected from 0, 1, 2, 3, 4, or 5 halogen atoms and 0, 1, or 2 groups selected from

(a) hydroxy;

(b) -COOH;

- (c)  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester, which may linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens;
- (d) a 5- or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen,  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl}$ , and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5 \text{ or } -\text{OC}_6 \text{ alkyl}$ , said  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl}$ , and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5 \text{ or } -\text{OC}_6 \text{ alkyl}$  being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.;
- (e) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (i) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (ii) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen,  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl}$ , and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5 \text{ or } -\text{OC}_6 \text{ alkyl}$ , said  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl}$ , and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5 \text{ or } -\text{OC}_6 \text{ alkyl}$  being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;
- (f)  $-\text{CONR}^{1025}\text{R}^{1025}$ ;
- (g)  $-\text{SO}_2\text{NR}^{1025}\text{R}^{1025}$ ;
- (h)  $-\text{NR}^{1025}-\text{C}(=\text{O})\text{R}^{1025}$ ;
- (i)  $-\text{NR}^{1025}-\text{C}(=\text{O})\text{NR}^{1025}\text{R}^{1025}$ ;
- (j)  $-\text{NR}^{1025}\text{COOR}^{1030}$ ;
- (k)  $-\text{O}-\text{CO}-\text{R}^{1030}$ ;
- (l)  $-\text{O}-\text{CO}-\text{NR}^{1025}\text{R}^{1025}$ ;
- (m)  $-\text{NR}^{1025}\text{SO}_2\text{R}^{1030}$ ;
- (n)  $-\text{NR}^{1025}\text{R}^{1025}$ ;
- (o) phenyl which is optionally substituted with 1, 2, 3, 4, or 5 group independently selected from halogen, hydroxy,  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl}$ ,  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5 \text{ or } -\text{OC}_6 \text{ alkyl}$ ,  $-\text{COOH}$ ,  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester, said  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl}$ ,  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5 \text{ or } -\text{OC}_6 \text{ alkyl}$ ,  $-\text{COOH}$ ,  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester being linear or branched and optionally substituted

with 1, 2, 3, 4, 5, or 6 substituents independently selected from 0 or 1

C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl and 0, 1, 2, 3, 4, or 5 halogens, and

(p) C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, which is optionally substituted with 1, 2, 3, 4, 5, or 6 halogens;

(5) OC<sub>1</sub>, OC<sub>2</sub>, OC<sub>3</sub>, OC<sub>4</sub>, OC<sub>5</sub>, OC<sub>6</sub>, OC<sub>7</sub>, OC<sub>8</sub>, OC<sub>9</sub> or OC<sub>10</sub> alkyl, which is linear or branched and is optionally substituted with 0, 1, 2, 3, 4, or 5 halogen atoms and 0, 1, or 2 substituents selected from

(a) hydroxy;

(b) -COOH;

(c) -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, which may be linear or branched and is optionally substituted with 1, 2, 3, 4 or 5 halogens;

(d) a 5- or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.;

(e) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (i) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (ii) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(f) -CONR<sup>1025</sup>R<sup>1025</sup>;

(g) -SO<sub>2</sub>NR<sup>1025</sup>R<sup>1025</sup>;

(h) -NR<sup>1025</sup>-C(=O)R<sup>1025</sup>

(i) -NR<sup>1025</sup>-C(=O)NR<sup>1025</sup>R<sup>1025</sup>;

(j) -NR<sup>1025</sup>COOR<sup>1030</sup>

(k) -O-CO-R<sup>1030</sup>

(l)  $-O-CO-NR^{1025}R^{1025}$ ;

(m)  $-NR^{1025}SO_2R^{1030}$ ;

(n)  $-NR^{1025}R^{1025}$ ;

(o) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5 groups independently selected from halogen, hydroxy,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl,  $-OC_1$ ,  $-OC_2$ ,  $-OC_3$ ,  $-OC_4$ ,  $-OC_5$  or  $-OC_6$  alkyl,  $-COOH$ ,  $-COO(C_1, C_2, C_3, C_4, C_5$  or  $C_6$  alkyl) i.e. ester, said  $C_1, C_2, C_3, C_4, C_5$  or  $C_6$  alkyl,  $-OC_1$ ,  $-OC_2$ ,  $-OC_3$ ,  $-OC_4$ ,  $-OC_5$  or  $-OC_6$  alkyl,  $-COOH$ ,  $-COO(C_1, C_2, C_3, C_4, C_5$  or  $C_6$  alkyl) i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, 5, or 6 substituents independently selected from 0 or 1  $C_3, C_4, C_5$  or  $C_6$  cycloalkyl and 0, 1, 2, 3, 4, or 5 halogens, and

(p)  $C_3, C_4, C_5$  or  $C_6$  cycloalkyl, which is optionally substituted with 1, 2, 3, 4, 5, or 6 halogens;

(6)  $-COOH$ ;

(7)  $-COO(C_1, C_2, C_3, C_4, C_5$  or  $C_6$  alkyl) i.e. ester, which may be linear or branched and is optionally substituted with 1, 2, 3, 4, 5 halogens;

(8) a 5- or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, said heterocycle being optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen,  $C_1, C_2, C_3, C_4, C_5$  or  $C_6$  alkyl, and  $-OC_1, -OC_2, -OC_3, -OC_4, -OC_5$  or  $-OC_6$  alkyl, said  $C_1, C_2, C_3, C_4, C_5$  or  $C_6$  alkyl, and  $-OC_1, -OC_2, -OC_3, -OC_4, -OC_5$  or  $-OC_6$  alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.

(9) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (a) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (b) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen,  $C_1, C_2, C_3, C_4, C_5$  or  $C_6$  alkyl, and  $-OC_1, -OC_2, -OC_3, -OC_4, -OC_5$  or  $-OC_6$  alkyl, said  $C_1, C_2, C_3, C_4, C_5$  or  $C_6$  alkyl, and  $-OC_1, -OC_2, -OC_3, -OC_4, -OC_5$  or  $-OC_6$  alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(10)  $-CONR^{1025}R^{1025}$ ;

(11)  $-SO_2NR^{1025}R^{1025}$ ;

(12)  $-NR^{1025}-C(=O)R^{1025}$

(13)  $-NR^{1025}-C(=O)NR^{1025}R^{1025}$ ,

(14)  $-NR^{925}COOR^{1030}$

(15)  $-O-CO-R^{1030}$

(16)  $-O-CO-NR^{1025}R^{1025}$ ,

(17)  $-NR^{1025}SO_2R^{1030}$ ,

(18)  $-NR^{1025}R^{1025}$ ,

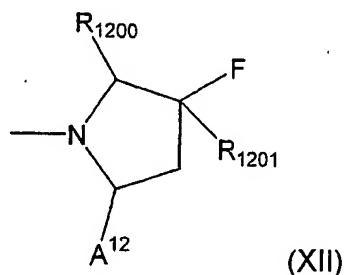
(19) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5 group independently selected from halogen, hydroxy,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl,  $-OC_1$ ,  $-OC_2$ ,  $-OC_3$ ,  $-OC_4$ ,  $-OC_5$  or  $-OC_6$  alkyl,  $-COOH$ ,  $-COO(C_1, C_2, C_3, C_4, C_5$  or  $C_6$  alkyl) i.e. ester, said  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl,  $-OC_1$ ,  $-OC_2$ ,  $-OC_3$ ,  $-OC_4$ ,  $-OC_5$  or  $-OC_6$  alkyl,  $-COOH$ ,  $-COO(C_1, C_2, C_3, C_4, C_5$  or  $C_6$  alkyl) i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein  $R^{1030}$  is selected from the group consisting of phenyl,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  cycloalkyl, and  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  cycloalkyl, wherein  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6, substituents independently selected from 0, 1, 2, 3, 4, or 5 halogens, 0 or 1 phenyl, wherein said optional phenyl substituent and said  $R^{930}$ , when  $R^{930}$  is phenyl or  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  cycloalkyl, are optionally substituted with 1, 2, 3, 4, or 5 substituents, independently selected from halogen, OH,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , or  $C_5$  alkyl,  $-OC_1$ ,  $-OC_2$ ,  $-OC_3$ ,  $-OC_4$ , or  $-OC_5$  alkyl, said  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , or  $C_5$  alkyl,  $-OC_1$ ,  $-OC_2$ ,  $-OC_3$ ,  $-OC_4$ , or  $-OC_5$  alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.

wherein  $R^{1025}$  is selected from  $R^{1030}$  and hydrogen.

or wherein the group PM

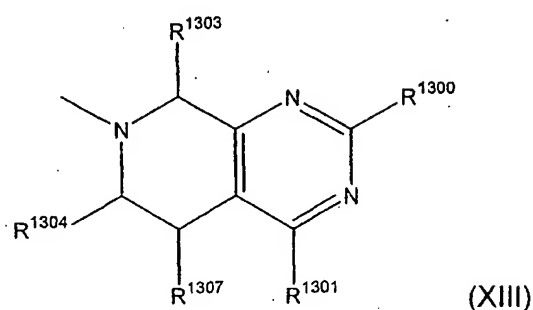
has the formula (XII)



- wherein the groups  $R^{1201}$  is hydrogen or fluoro.
- wherein  $R^{1200}$  und  $A^{12}$  is selected from hydrogen and cyano, and the other is hydrogen.

or wherein the group **PM**

has the formula XIII:



wherein:

$R^{1300}$  and  $R^{1301}$  are independently selected from the group consisting of:

- (1) hydrogen,
- (2) CN,
- (3)  $C_{1-10}$ alkyl, which is linear or branched which is unsubstituted or substituted with:
  - a) halogen, or
  - b) phenyl, which is unsubstituted or substituted with 1 - 5 substituents independently selected from halogen, CN, OH,  $R^{1302}$ ,  $OR^{1302}$ ,  $NHSO_2R^{1302}$ ,  $N(C_{1-6}alkyl)SO_2R^{1302}$ ,  $SO_2R^{1302}$ ,  $SO_2NR^{1305}R^{1306}$ ,  $NR^{1305}R^{1306}$ ,  $CONR^{1305}R^{1306}$ ,  $CO_2H$ , and  $CO_2C_{1-6}alkyl$ , wherein the  $C_{1-6}alkyl$  is linear or branched,
- (4) phenyl which is unsubstituted or substituted with 1 - 5 substituents independently selected from halogen, CN, OH,  $R^{1302}$ ,  $OR^{1302}$ ,  $NHSO_2R^{1302}$ ,

$N(C_{1-6}\text{alkyl})SO_2R^{1302}$ ,  $SO_2R^{1302}$ ,  $SO_2NR^{1305}R^{1306}$ ,  $NR^{1305}R^{1306}$ ,  $CONR^{1305}R^{1306}$ ,  $CO_2H$ , and  $CO_2C_{1-6}\text{alkyl}$ , wherein the  $C_{1-6}\text{alkyl}$  is linear or branched,

- (5) a 5- or 6-membered heterocyclic which may be saturated or unsaturated comprising 1 – 4 heteroatoms independently selected from N, S and O, the heterocycle being unsubstituted or substituted with 1 – 3 substituents independently selected from oxo, halogen,  $NO_2$ , CN, OH,  $R^{1302}$ ,  $OR^{1302}$ ,  $NHSO_2R^{1302}$ ,  $N(C_{1-6}\text{alkyl})SO_2R^{1302}$ ,  $SO_2R^{1302}$ ,  $SO_2NR^{1305}R^{1306}$ ,  $NR^{1305}R^{1306}$ ,  $CONR^{1305}R^{1306}$ ,  $CO_2H$ , and  $CO_2C_{1-6}\text{alkyl}$ , wherein the  $C_{1-6}\text{alkyl}$  is linear or branched,
- (6)  $C_{3-6}\text{cycloalkyl}$ , which is optionally substituted with 1 – 5 substituents independently selected from halogen, OH,  $C_{1-6}\text{alkyl}$ , and  $OC_{1-6}\text{alkyl}$ , wherein the  $C_{1-6}\text{alkyl}$  and  $OC_{1-6}\text{alkyl}$  are linear or branched and optionally substituted with 1 – 5 halogens,
- (7) OH,
- (8)  $OR^{1302}$ , and
- (9)  $NR^{1305}R^{1306}$ ,

$R^{1302}$  is  $C_{1-6}\text{alkyl}$ , which is linear or branched and which is unsubstituted or substituted with 1 – 5 groups independently selected from halogen,  $CO_2H$ , and  $CO_2C_{1-6}\text{alkyl}$ , wherein the  $C_{1-6}\text{alkyl}$  is linear or branched;

$R^{1303}$ ,  $R^{1304}$  and  $R^{1307}$  are independently selected from the group consisting of:

- (1) hydrogen,
- (2)  $C_{1-10}\text{alkyl}$ , which is linear or branched and which is unsubstituted or substituted with one or more substituted selected from:
  - a) halogen,
  - b) hydroxy,
  - c) phenyl, which is unsubstituted or substituted with 1 – 5 substituted independently selected from halogen, OH,  $C_{1-6}\text{alkyl}$ , and  $OC_{1-6}\text{alkyl}$ , wherein the  $C_{1-6}\text{alkyl}$  is linear or branched and optionally substituted with 1 – 5 halogens,

- d) naphthyl, wherein the naphthyl is optionally substituted with 1 – 5 substituents independently selected from halogen, OH, C<sub>1-6</sub>alkyl, and OC<sub>1-6</sub>alkyl, wherein the C<sub>1-6</sub>alkyl is linear or branched and optionally substituted with 1 – 5 halogens,
  - e) CO<sub>2</sub>H,
  - f) CO<sub>2</sub>C<sub>1-6</sub>alkyl,
  - g) CONR<sup>1305</sup>R<sup>1306</sup>,
- (3) CN,
  - (4) phenyl which is unsubstituted or substituted with 1 – 5 substituents independently selected from C<sub>1-6</sub>alkyl, and OC<sub>1-6</sub>alkyl, hydroxy and halogen, wherein the C<sub>1-6</sub>alkyl is linear or branched and optionally substituted with 1 – 5 halogens,
  - (5) naphthyl which is unsubstituted or substituted with 1 – 5 substituents independently selected from C<sub>1-6</sub>alkyl, and OC<sub>1-6</sub>alkyl, hydroxy and halogen, wherein the C<sub>1-6</sub>alkyl is linear or branched and optionally substituted with 1 – 5 halogens,
  - (6) CO<sub>2</sub>H,
  - (7) CO<sub>2</sub>C<sub>1-6</sub>alkyl,
  - (8) CONR<sup>1305</sup>R<sup>1306</sup>, and
  - (9) C<sub>3-6</sub>cycloalkyl, which is unsubstituted or substituted with 1 – 5 substituents independently selected from C<sub>1-6</sub>alkyl, and OC<sub>1-6</sub>alkyl, hydroxy and halogen, wherein the C<sub>1-6</sub>alkyl is linear or branched and optionally substituted with 1 – 5 halogens;

R<sup>1305</sup> and R<sup>1306</sup> are independently selected from the group consisting of:

- (1) hydrogen,
- (2) phenyl, which is unsubstituted or substituted with substituents independently selected from halogen, OH, C<sub>1-6</sub>alkyl, and OC<sub>1-6</sub>alkyl, wherein the C<sub>1-6</sub>alkyl is linear or branched and optionally substituted with 1 – 5 halogens;



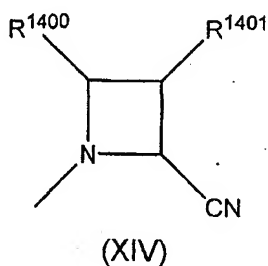
- (3) C<sub>3-6</sub>cycloalkyl, which is unsubstituted or substituted with 1 – 5 substituents independently selected from C<sub>1-6</sub>alkyl; and OC<sub>1-6</sub>alkyl, wherein the C<sub>1-6</sub>alkyl is linear or branched and optionally substituted with 1 – 5 halogens,
- (4) C<sub>1-6</sub>alkyl, which is linear or branched and which is unsubstituted or substituted with:

- a) halogen, or
- b) phenyl, which is unsubstituted or substituted with 1 – 5 substituents independently selected from halogen, OH, C<sub>1-6</sub>alkyl, and OC<sub>1-6</sub>alkyl, wherein the C<sub>1-6</sub>alkyl is linear or branched and optionally substituted with 1 – 5 halogens,

or wherein R<sup>1305</sup> and R<sup>1306</sup> together with the nitrogen atom to which they are attached form a heterocyclic ring selected from azetidine, pyrrolidine, piperidine, piperazine, and morpholine wherein said heterocyclic ring is unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, C<sub>1-6</sub>alkyl, and C<sub>1-6</sub>alkoxy, wherein alkyl and alkoxy are unsubstituted with one to five halogens;

or wherein the group PM

has the formula XIV:



- wherein R<sup>1400</sup> and R<sup>1401</sup>, independently of each other, are
- a hydrogen atom (-H); or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group or, a carbaldehyde (-CHO), a ketone

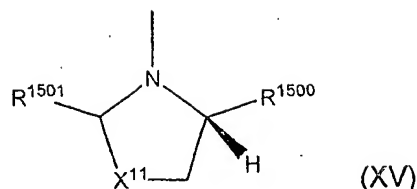
group ( $-\text{CO}-\text{R}^{1402}$ ), a **boronic acid** group ( $-\text{B}(\text{OH})_2$ ), a **cyano** group ( $-\text{C}\equiv\text{N}$ ), a **carboxylic acid** group ( $-\text{COOH}$ ), a **carboxylic acid ester** group ( $-\text{COOR}^{1403}$ ), a **carboxylic acid anhydride** group ( $-\text{CO}-\text{O}-\text{CO}-\text{R}^{1404}$ ), a **hydroxamic acid** group ( $-\text{CO}-\text{NH}(\text{OH})$ ), a **N-substituted hydroxamic acid** group ( $-\text{CO}-\text{NR}^{1405}(\text{OH})$ ), a **O-substituted hydroxamic acid** group ( $-\text{CO}-\text{NH}(\text{OR}^{1406})$ ), a **carboxamide** group ( $-\text{CO}-\text{NH}_2$ ), a **N-substituted or N,N-disubstituted carboxylic acid amide** group, ( $-\text{CO}-\text{NHR}^{1407}$ ;  $-\text{CO}-\text{NR}^{1408}\text{R}^{1409}$ ), an **amido group** ( $-\text{HN}-\text{CO}-\text{R}^{1410}$ ), a **sulfonic acid** group ( $-\text{SO}_3\text{H}$ ), a **sulfonamide** group ( $-\text{SO}_2-\text{NH}_2$ ), a **N-substituted or N,N-disubstituted sulfonamide** group ( $-\text{SO}_2-\text{NHR}^{1411}$ ;  $-\text{SO}_2-\text{NR}^{1412}\text{R}^{1413}$ ), an **amidosulfone** group ( $-\text{NH}-\text{SO}_2-\text{R}^{1414}$ ), a **sulfone** group ( $-\text{SO}_2-\text{R}^{1415}$ ), a **phosphoric acid** group ( $-\text{OP}(=\text{O})(\text{OH})_2$ ), a **phosphoric acid ester** group ( $-\text{OP}(=\text{O})(\text{OR}^{1416})(\text{OR}^{1417})$ ), a **phosphonic acid** group ( $-\text{P}(=\text{O})(\text{OH})_2$ ), an **phosphonic acid ester** group ( $-\text{P}(=\text{O})(\text{OR}^{1418})(\text{OR}^{1419})$ ), a **halogen atom**, a **trifluormethyl** group ( $-\text{CF}_3$ ), a **thiol** group ( $-\text{SH}$ ); a **thioether** group ( $-\text{S}-\text{R}^{1420}$ ), a **hydroxy** group ( $-\text{OH}$ ); an **alkoxy** group ( $-\text{O}-\text{R}^{1421}$ ), a **tetrazole** group, an **amino** group ( $-\text{NH}_2$ ), or a **N-substituted or N,N-disubstituted amino** group ( $-\text{NHR}^{1422}$ ;  $-\text{NR}^{1423}\text{R}^{1424}$ ); and

- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; and,
- wherein optionally, the pairs  $\text{R}^{1408}/\text{R}^{1409}$ ,  $\text{R}^{1412}/\text{R}^{1413}$ ,  $\text{R}^{1416}/\text{R}^{1417}$ ,  $\text{R}^{1418}/\text{R}^{1419}$  and  $\text{R}^{1423}/\text{R}^{1424}$ , independently of each other, may form a part of a **ring**; and

- wherein the substituents  $\text{R}^{1402}$ ,  $\text{R}^{1403}$ ,  $\text{R}^{1404}$ ,  $\text{R}^{1405}$ ,  $\text{R}^{1406}$ ,  $\text{R}^{1407}$ ,  $\text{R}^{1408}$ ,  $\text{R}^{1409}$ ,  $\text{R}^{1410}$ ,  $\text{R}^{1411}$ ,  $\text{R}^{1412}$ ,  $\text{R}^{1413}$ ,  $\text{R}^{1414}$ ,  $\text{R}^{1415}$ ,  $\text{R}^{1416}$ ,  $\text{R}^{1417}$ ,  $\text{R}^{1418}$ ,  $\text{R}^{1419}$ ,  $\text{R}^{1420}$ ,  $\text{R}^{1421}$ ,  $\text{R}^{1422}$ ,  $\text{R}^{1423}$ , and  $\text{R}^{1424}$ , independently of each other are a **hydrogen atom** ( $-\text{H}$ ), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

or wherein the group PM

has the formula XV:

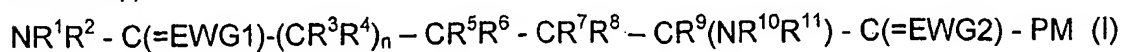


- wherein  $X^{11}$  is  $CH_2$ ,  $CHF$  or  $CF_2$ ;
- wherein  $R^{1500}$  is selected from the group consisting of alkylcarbonyl, arylcarbonyl, cyano, heterocyclecarbonyl,  $R^{1502}R^{1503}NC(O)-$ ,  $B(OR^{1504})_2$ , (1,2,3)-dioxaborolane and 4,4,5,5-tetramethyl(1,2,3)-dioxaborolane;
- wherein  $R^{1501}$  is selected from the group consisting of alkoxyalkyl, alkyl, alkylcarbonyl, alkenyl, alkynyl, allenyl, arylalkyl, cycloalkyl, cycloalkylalkyl, cyano, haloalkyl, haloalkenyl, heterocyclealkyl, and hydroxyalkyl;
- wherein  $R^{1502}$ ,  $R^{1503}$  and  $R^{1504}$  are each independently selected from the group consisting of hydrogen, alkyl, and arylalkyl;

with the proviso that the following compounds are excluded:

glutamin-thiazolidin (=Gln-Thia), glutamin-pyrrolidin (=Gln-Pyrr) (from WO 03/072556), glutamin-pyrrolidin-2-carboxylic acid (= Gln-Pro), glutamin-pyrrolidin-2-carboxamid (=Gln-Pro amid), and (S,S) 4-Amino-5-(2-cyano-2,5-dihydro-pyrrol-1-yl)-6-oxo-pentanoic acid amide (Gln - 2-cyano-2,5-dihydro-pyrrolidin) (from WO 01/55105).

In a further embodiment, the present invention comprises a compound of the general formula (I)



wherein n is 0 or 1;

wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ , and  $R^{11}$  independently of each other are

- a **hydrogen** atom; or
- a substituted or unsubstituted **alkyl** group having 1 to 30 carbon atoms; or
- a substituted or unsubstituted **alkenyl** group having 2 to 30 carbon atoms; or
- a substituted or unsubstituted **alkinyl** group having 2 to 30 carbon atoms; or
- a substituted or unsubstituted **cycloalkyl** group having 3 to 30 carbon atoms; or
- a substituted or unsubstituted **cycloalkenyl** group having 3 to 30 carbon atoms;
- or a substituted or unsubstituted **cycloalkinyl** group having 6 to 30 carbon atoms;
- or
- a substituted or unsubstituted **heteroalkyl** group having 1 to 30 carbon atoms and 1 to 6 hetero atoms each independently selected from oxygen, nitrogen or sulfur; or
- a substituted or unsubstituted **heteroalkenyl** group having 2 to 30 carbon atoms and 1 to 6 hetero atoms each independently selected from oxygen, nitrogen or sulfur; or
- a substituted or unsubstituted **heteroalkinyl** group having 2 to 30 carbon atoms and 1 to 6 hetero atoms each independently selected from oxygen, nitrogen or sulfur; or
- a substituted or unsubstituted **heterocycloalkyl** group having 1 to 30 carbon atoms, and 1 to 6 hetero atoms each independently selected from oxygen, nitrogen or sulfur; or
- a substituted or unsubstituted **heterocycloalkenyl** group having 2 to 30 carbon atoms, and 1 to 6 hetero atoms each independently selected from oxygen, nitrogen or sulfur; or
- a substituted or unsubstituted **aryl** group having 3 to 30 carbon atoms; or
- a substituted or unsubstituted **heteroaryl** group having 1 to 30 carbon atoms, and 1 to 10 hetero atoms, each independently selected from oxygen, nitrogen or sulfur; or
- a substituted or unsubstituted **aryl-alkyl** group having at least one substituted or unsubstituted aryl group each having 1 to 30 carbon atoms, and at least one substituted or unsubstituted alkyl group each having 1 to 30 carbon atoms; or

- a substituted or unsubstituted **heteroaryl-alkyl** group having at least one substituted or unsubstituted heteroaryl group each having 1 to 30 carbon atoms, and 1 to 10 hetero atoms, each independently selected from oxygen, nitrogen or sulfur, and further, at least one substituted or unsubstituted alkyl group having 1 to 30 carbon atoms; or
- a substituted or unsubstituted **aryl-heteroalkyl** group having at least one substituted or unsubstituted aryl group each having 3 to 30 carbon atoms, and at least one substituted or unsubstituted heteroalkyl group each having 1 to 30 carbon atoms and 1 to 6 hetero atoms each independently selected from oxygen, nitrogen or sulfur; or
- a substituted or unsubstituted **heteroaryl-heteroalkyl** group having at least one substituted or unsubstituted heteroaryl group each having 1 to 30 carbon atoms, and 1 to 10 hetero atoms, each independently selected from oxygen, nitrogen or sulfur, and further, at least one substituted or unsubstituted heteroalkyl group each having 1 to 30 carbon atoms and 1 to 6 hetero atoms each independently selected from oxygen, nitrogen or sulfur; or
- a **carbaldehyde** (-CHO), a **ketone** group (-CO-R<sup>20</sup>), a **boronic acid** group (-B(OH)<sub>2</sub>), a **cyano** group (-C≡N), a **carboxylic acid** group (-COOH), a **carboxylic acid ester** group (-COOR<sup>21</sup>), a **carboxylic acid anhydride** group (-CO-O-CO-R<sup>22</sup>), a **hydroxamic acid** group (-CO-NH(OH)), a N-substituted **hydroxamic acid** group (-CO-NR<sup>23</sup>(OH)), a O-substituted **hydroxamic acid** group (-CO-NH(OR<sup>24</sup>)), a **carboxamide** group (-CO-NH<sub>2</sub>), a N-substituted or N,N-disubstituted **carboxylic acid amide** group, (-CO-NHR<sup>25</sup>; -CO-NR<sup>26</sup>R<sup>27</sup>), an **amido** group (-HN-CO-R<sup>28</sup>), a **sulfonic acid** group (-SO<sub>3</sub>H), a **sulfonamide** group (-SO<sub>2</sub>-NH<sub>2</sub>), a N-substituted or N,N-disubstituted **sulfonamide** group (-SO<sub>2</sub>-NHR<sup>29</sup>; -SO<sub>2</sub>-NR<sup>30</sup>R<sup>31</sup>), an **amidosulfone** group (-NH-SO<sub>2</sub>-R<sup>32</sup>), a **sulfone** group (-SO<sub>2</sub>-R<sup>33</sup>), a **phosphoric acid** group (-OP(=O)(OH)<sub>2</sub>), a **phosphoric acid ester** group (-OP(=O)(OR<sup>34</sup>)(OR<sup>35</sup>)), a **phosphonic acid** group (-P(=O)(OH)<sub>2</sub>), an **phosphonic acid ester** group (-P(=O)(OR<sup>36</sup>)(OR<sup>37</sup>)), a **halogen atom**, a **trifluormethyl** group (-CF<sub>3</sub>), a **thiol** group (-SH); a **thioether** group (-S-R<sup>38</sup>), a **hydroxy** group (-OH); an **alkoxy** group (-O-R<sup>39</sup>), a **tetrazole** group, an **amino**

group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted **amino** group (-NHR<sup>40</sup>; -NR<sup>41</sup>R<sup>42</sup>);

- which each independently can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, any **two of the groups** R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup>, and R<sup>11</sup>, as well the pairs R<sup>26</sup>/R<sup>27</sup>, R<sup>30</sup>/R<sup>31</sup>, R<sup>34</sup>/R<sup>35</sup>, R<sup>36</sup>/R<sup>37</sup> and R<sup>41</sup>/R<sup>42</sup>, independently of each other, may form a part of a **ring**; and
  - wherein the substituents R<sup>20</sup>, R<sup>21</sup>, R<sup>22</sup>, R<sup>23</sup>, R<sup>24</sup>, R<sup>25</sup>, R<sup>26</sup>, R<sup>27</sup>, R<sup>28</sup>, R<sup>29</sup>, R<sup>30</sup>, R<sup>31</sup>, R<sup>32</sup>, R<sup>33</sup>, R<sup>34</sup>, R<sup>35</sup>, R<sup>36</sup>, R<sup>37</sup>, R<sup>38</sup>, R<sup>39</sup>, R<sup>40</sup>, R<sup>41</sup>, and R<sup>42</sup> independently of each other are a **hydrogen** atom (-H), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group.

In a further embodiment, the present invention comprises a compound of the general formula (I)



wherein n is 0 or 1;

wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup>, and R<sup>11</sup> independently of each other are

- a **hydrogen** atom; or
- a substituted or unsubstituted **alkyl** group having 1 to 20 carbon atoms; or
- a substituted or unsubstituted **alkenyl** group having 2 to 20 carbon atoms; or
- a substituted or unsubstituted **alkinyl** group having 2 to 20 carbon atoms; or
- a substituted or unsubstituted **cycloalkyl** group having 3 to 20 carbon atoms; or
- a substituted or unsubstituted **cycloalkenyl** group having 3 to 20 carbon atoms;

- or a substituted or unsubstituted **cycloalkinyl** group having 6 to 20 carbon atoms;  
or
- a substituted or unsubstituted **heteroalkyl** group having 1 to 20 carbon atoms and 1 to 3 hetero atoms each independently selected from oxygen, nitrogen or sulfur; or
- a substituted or unsubstituted **heteroalkenyl** group having 2 to 20 carbon atoms and 1 to 3 hetero atoms each independently selected from oxygen, nitrogen or sulfur; or
- a substituted or unsubstituted **heteroalkinyl** group having 2 to 20 carbon atoms and 1 to 3 hetero atoms each independently selected from oxygen, nitrogen or sulfur; or
- a substituted or unsubstituted **heterocycloalkyl** group having 1 to 20 carbon atoms, and 1 to 3 hetero atoms each independently selected from oxygen, nitrogen or sulfur; or
- a substituted or unsubstituted **heterocycloalkenyl** group having 2 to 20 carbon atoms, and 1 to 3 hetero atoms each independently selected from oxygen, nitrogen or sulfur; or
- a substituted or unsubstituted **aryl** group having 3 to 20 carbon atoms; or
- a substituted or unsubstituted **heteroaryl** group having 1 to 20 carbon atoms, and 1 to 4 hetero atoms, each independently selected from oxygen, nitrogen or sulfur;  
or
- a substituted or unsubstituted **aryl-alkyl** group having at least one substituted or unsubstituted aryl group each having 1 to 20 carbon atoms, and at least one substituted or unsubstituted alkyl group each having 1 to 20 carbon atoms; or
- a substituted or unsubstituted **heteroaryl-alkyl** group having at least one substituted or unsubstituted heteroaryl group each having 1 to 20 carbon atoms, and 1 to 4 hetero atoms, each independently selected from oxygen, nitrogen or sulfur, and further, at least one substituted or unsubstituted alkyl group having 1 to 20 carbon atoms; or
- a substituted or unsubstituted **aryl-heteroalkyl** group having at least one substituted or unsubstituted aryl group each having 3 to 20 carbon atoms, and at least one substituted or unsubstituted heteroalkyl group each having 1 to 20

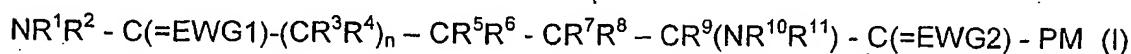
carbon atoms and 1 to 3 hetero atoms each independently selected from oxygen, nitrogen or sulfur; or

- a substituted or unsubstituted **heteroaryl-heteroalkyl** group having at least one substituted or unsubstituted heteroaryl group each having 1 to 20 carbon atoms, and 1 to 4 hetero atoms, each independently selected from oxygen, nitrogen or sulfur, and further, at least one substituted or unsubstituted heteroalkyl group each having 1 to 20 carbon atoms and 1 to 4 hetero atoms each independently selected from oxygen, nitrogen or sulfur; or
- a **carbaldehyde** (-CHO), a **ketone** group (-CO-R<sup>20</sup>), a **boronic acid** group (-B(OH)<sub>2</sub>), a **cyano** group (-C≡N), a **carboxylic acid** group (-COOH), a **carboxylic acid ester** group (-COOR<sup>21</sup>), a **carboxylic acid anhydride** group (-CO-O-CO-R<sup>22</sup>), a **hydroxamic acid** group (-CO-NH(OH)), a N-substituted **hydroxamic acid** group (-CO-NR<sup>23</sup>(OH)), a O-substituted **hydroxamic acid** group (-CO-NH(OR<sup>24</sup>)), a **carboxamide** group (-CO-NH<sub>2</sub>), a N-substituted or N,N-disubstituted **carboxylic acid amide** group, (-CO-NHR<sup>25</sup>; -CO-NR<sup>26</sup>R<sup>27</sup>), an **amido** group (-HN-CO-R<sup>28</sup>), a **sulfonic acid** group (-SO<sub>3</sub>H), a **sulfonamide** group (-SO<sub>2</sub>-NH<sub>2</sub>), a N-substituted or N,N-disubstituted **sulfonamide** group (-SO<sub>2</sub>-NHR<sup>29</sup>; -SO<sub>2</sub>-NR<sup>30</sup>R<sup>31</sup>), an **amidosulfone** group (-NH-SO<sub>2</sub>-R<sup>32</sup>), a **sulfone** group (-SO<sub>2</sub>-R<sup>33</sup>), a **phosphoric acid** group (-OP(=O)(OH)<sub>2</sub>), a **phosphoric acid ester** group (-OP(=O)(OR<sup>34</sup>)(OR<sup>35</sup>)), a **phosphonic acid** group (-P(=O)(OH)<sub>2</sub>), an **phosphonic acid ester** group (-P(=O)(OR<sup>36</sup>)(OR<sup>37</sup>)), a **halogen atom**, a **trifluormethyl** group (-CF<sub>3</sub>), a **thiol** group (-SH), a **thioether** group (-S-R<sup>38</sup>), a **hydroxy** group (-OH), an **alkoxy** group (-O-R<sup>39</sup>), a **tetrazole** group, an **amino** group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted **amino** group (-NHR<sup>40</sup>; -NR<sup>41</sup>R<sup>42</sup>);
- which each independently can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, any **two of the groups** R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup>, and R<sup>11</sup>, as well the pairs R<sup>26</sup>/R<sup>27</sup>, R<sup>30</sup>/R<sup>31</sup>, R<sup>34</sup>/R<sup>35</sup>, R<sup>36</sup>/R<sup>37</sup> and R<sup>41</sup>/R<sup>42</sup>, independently of each other, may form a part of a **ring**; and



- wherein the substituents  $R^{20}$ ,  $R^{21}$ ,  $R^{22}$ ,  $R^{23}$ ,  $R^{24}$ ,  $R^{25}$ ,  $R^{26}$ ,  $R^{27}$ ,  $R^{28}$ ,  $R^{29}$ ,  $R^{30}$ ,  $R^{31}$ ,  $R^{32}$ ,  $R^{33}$ ,  $R^{34}$ ,  $R^{35}$ ,  $R^{36}$ ,  $R^{37}$ ,  $R^{38}$ ,  $R^{39}$ ,  $R^{40}$ ,  $R^{41}$ , and  $R^{42}$  independently of each other are a hydrogen atom (-H), or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group.

In a preferred embodiment, the present invention comprises a compound of the general formula (I)



wherein n is 0 or 1;

wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ , and  $R^{11}$  independently of each other are

- a hydrogen atom; or
- a straight or branched chain, substituted or unsubstituted alkyl group comprising methyl ( $-CH_3$ ) and ethyl ( $-C_2H_5$ ); or
- a halogen comprising a fluoro, chloro, bromo or iodo atom; or
- a cyano group; a thiol group; a hydroxy group; a carboxyl group, a tetrazole group, an amino group; an amido group;

and wherein EWG1 and EWG2 is a double bound oxygen (=O).

In a more preferred embodiment, the present invention comprises a compound of the general formula (I)

- wherein n is 0;
- wherein  $R^1$ ,  $R^2$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ , and  $R^{11}$ , is each a hydrogen atom; and
- wherein EWG1 and EWG2 is a double bound oxygen (=O).

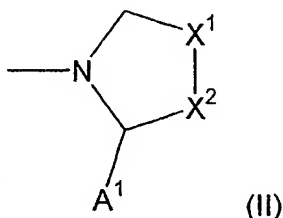
In a further more preferred embodiment, the present invention comprises a compound of the general formula (I)

- wherein n is 1;
- wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ , and  $R^{11}$  is each a hydrogen atom; and
- wherein EWG1 and EWG2 is a double bound oxygen (=O).

Preferred are compounds as disclosed above

wherein the group PM

has the formula (II)



- wherein  $X^1$  is  $CR^{51}R^{52}$ , O, S, or  $NR^{53}$ ; and
- wherein  $X^2$  is  $CR^{54}R^{55}$ , O, S, or  $NR^{56}$ ; and

wherein  $R^{51}$ ,  $R^{52}$ ,  $R^{53}$ ,  $R^{54}$ ,  $R^{55}$ , and  $R^{56}$ , independently of each other, are

- a **hydrogen** atom (-H); or an  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkenyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkinyl**,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  **cycloalkyl**,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  **cycloalkenyl**, **aryl**, **heteroaryl** or **amino** ( $-NH_2$ ), or a N-substituted or N,N-disubstituted **amino** group ( $-NHR^{80}$ ,  $-NR^{81}R^{82}$ ); and

- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, any **two of the groups**  $R^{51}$ ,  $R^{52}$ ,  $R^{53}$ ,  $R^{54}$ ,  $R^{55}$ , and  $R^{56}$ , if present, as well as the pairs  $R^{66}/R^{67}$ ,  $R^{70}/R^{71}$ ,  $R^{74}/R^{75}$ ,  $R^{76}/R^{77}$  and  $R^{81}/R^{82}$ , independently of each other, may form a part of a **ring**; and
- wherein the substituents  $R^{60}$ ,  $R^{61}$ ,  $R^{62}$ ,  $R^{63}$ ,  $R^{64}$ ,  $R^{65}$ ,  $R^{66}$ ,  $R^{67}$ ,  $R^{68}$ ,  $R^{69}$ ,  $R^{70}$ ,  $R^{71}$ ,  $R^{72}$ ,  $R^{73}$ ,  $R^{74}$ ,  $R^{75}$ ,  $R^{76}$ ,  $R^{77}$ ,  $R^{78}$ ,  $R^{79}$ ,  $R^{80}$ ,  $R^{81}$ , and  $R^{82}$ , independently of each other, are a **hydrogen atom** (-H), or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkyl**, **aryl**, **heteroaryl**, **amino**, **halo**, **carbonyl**,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkoxy**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkenoxy**, **phenyloxy**, **benzyloxy**,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  **cycloalkyl**, **ciano**, **amido**, **thiol** **trifluoromethyl**, or **hydroxy group**; and

wherein  $A^1$  is

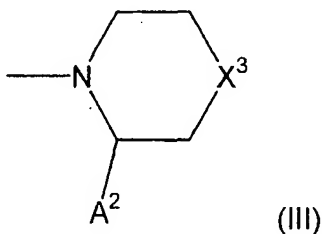
- a **hydrogen atom** (-H) or a **carbaldehyde** (-CHO), a **ketone group** (-CO- $R^{100}$ ), a **boronic acid group** (-B(OH)<sub>2</sub>), a **cyano group** (-C≡N), a **carboxylic acid group** (-COOH), a **carboxylic acid ester group** (-COOR<sup>101</sup>), a **carboxylic acid anhydride group** (-CO-O-CO- $R^{102}$ ), a **hydroxamic acid group** (-CO-NH(OH)), a **N-substituted hydroxamic acid group** (-CO-NR<sup>103</sup>(OH)), a **O-substituted hydroxamic acid group** (-CO-NH(OR<sup>104</sup>)), a **carboxamide group** (-CO-NH<sub>2</sub>), a **N-substituted or N,N-disubstituted carboxylic acid amide group**, (-CO-NHR<sup>105</sup>, -CO-NR<sup>106</sup>R<sup>107</sup>), an **amido group** (-HN-CO- $R^{108}$ ), a **sulfonic acid group** (-SO<sub>3</sub>H), a **sulfonamide group** (-SO<sub>2</sub>-NH<sub>2</sub>), a **N-substituted or N,N-disubstituted sulfonamide group** (-SO<sub>2</sub>-NHR<sup>109</sup>, -SO<sub>2</sub>-NR<sup>110</sup>R<sup>111</sup>), an **amidosulfone group** (-NH-SO<sub>2</sub>- $R^{112}$ ), a **sulfone group** (-SO<sub>2</sub>- $R^{113}$ ), a **phosphoric acid group** (-OP(=O)(OH)<sub>2</sub>), a **phosphoric acid ester group** (-OP(=O)(OR<sup>114</sup>)(OR<sup>115</sup>)), a **phosphonic acid group** (-P(=O)(OH)<sub>2</sub>), an **phosphonic acid ester group** (-P(=O)(OR<sup>116</sup>)(OR<sup>117</sup>)), a **halogen atom**, a **trifluormethyl group** (-CF<sub>3</sub>), a **thiol**

group (-SH); a **thioether** group (-S-R<sup>118</sup>), a **hydroxy** group (-OH); an **alkoxy** group (-O-R<sup>119</sup>), a **tetrazole** group, an **amino** group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted **amino** group (-NHR<sup>120</sup>, -NR<sup>121</sup>R<sup>122</sup>); and

- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the pairs R<sup>106</sup>/R<sup>107</sup>, R<sup>110</sup>/R<sup>111</sup>, R<sup>114</sup>/R<sup>115</sup>, R<sup>116</sup>/R<sup>117</sup> and R<sup>121</sup>/R<sup>122</sup>, independently of each other, may form a part of a **ring**; and
- wherein the substituents R<sup>100</sup>, R<sup>101</sup>, R<sup>102</sup>, R<sup>103</sup>, R<sup>104</sup>, R<sup>105</sup>, R<sup>106</sup>, R<sup>107</sup>, R<sup>108</sup>, R<sup>109</sup>, R<sup>110</sup>, R<sup>111</sup>, R<sup>112</sup>, R<sup>113</sup>, R<sup>114</sup>, R<sup>115</sup>, R<sup>116</sup>, R<sup>117</sup>, R<sup>118</sup>, R<sup>119</sup>, R<sup>120</sup>, R<sup>121</sup>, and R<sup>122</sup>, independently of each other, are a **hydrogen** atom (-H), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

or wherein the group **PM**

has the formula (III)



- wherein X<sup>3</sup> is CR<sup>131</sup>R<sup>132</sup>, O, S, or NR<sup>133</sup>; and
- wherein R<sup>131</sup>, R<sup>132</sup>, and R<sup>133</sup>, independently of each other, are
- a **hydrogen** atom (-H); or an C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub> and C<sub>9</sub> branched or straight chain **alkyl**, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub> and C<sub>9</sub> branched or straight chain

**alkenyl**, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub> and C<sub>9</sub> branched or straight chain **alkinyl**, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub> and C<sub>9</sub> **cycloalkyl**, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub> and C<sub>9</sub> **cycloalkenyl**, **aryl**, **heteroaryl** or an **amino** group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted **amino** group (-NHR<sup>160</sup>, -NR<sup>161</sup>R<sup>162</sup>); and

- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the **the pair** R<sup>131</sup>/R<sup>132</sup>, if present, as well the pairs R<sup>146</sup>/R<sup>147</sup>, R<sup>150</sup>/R<sup>151</sup>, R<sup>154</sup>/R<sup>155</sup>, R<sup>156</sup>/R<sup>157</sup> and R<sup>161</sup>/R<sup>162</sup>, independently of each other, may form a part of a **ring**; and
- wherein the substituents R<sup>140</sup>, R<sup>141</sup>, R<sup>142</sup>, R<sup>143</sup>, R<sup>144</sup>, R<sup>145</sup>, R<sup>146</sup>, R<sup>147</sup>, R<sup>148</sup>, R<sup>149</sup>, R<sup>150</sup>, R<sup>151</sup>, R<sup>152</sup>, R<sup>153</sup>, R<sup>154</sup>, R<sup>155</sup>, R<sup>156</sup>, R<sup>157</sup>, R<sup>158</sup>, R<sup>159</sup>, R<sup>160</sup>, R<sup>161</sup>, and R<sup>162</sup>, independently of each other are a **hydrogen** atom (-H), or a C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub> and C<sub>9</sub> branched or straight chain **alkyl**, **aryl**, **heteroaryl**, **amino**, **halo**, **carbonyl**, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub> and C<sub>9</sub> branched or straight chain **alkoxy**, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub> and C<sub>9</sub> branched or straight chain **alkenoxy**, **phenyloxy**, **benzyloxy**, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub> and C<sub>9</sub> **cycloalkyl**, **cyano**, **amido**, **thiol**, **trifluoromethyl**, or **hydroxy** group; and

wherein A<sup>2</sup> is

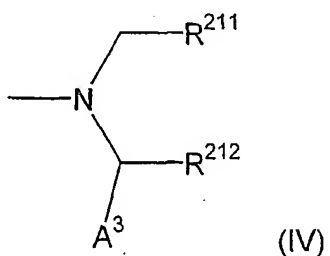
- a **hydrogen** atom (-H); or a **carbaldehyde** (-CHO), a **ketone** group (-CO-R<sup>180</sup>), a **boronic acid** group (-B(OH)<sub>2</sub>), a **cyano** group (-C≡N), a **carboxylic acid** group (-COOH), a **carboxylic acid ester** group (-COOR<sup>181</sup>), a **carboxylic acid anhydride** group (-CO-O-CO-R<sup>182</sup>), a **hydroxamic acid** group (-CO-NH(OH)), a N-substituted **hydroxamic acid** group (-CO-NR<sup>183</sup>(OH)), a O-substituted **hydroxamic acid** group (-CO-NH(OR<sup>184</sup>)), a **carboxamide** group (-CO-NH<sub>2</sub>), a N-substituted or N,N-disubstituted **carboxylic acid amide** group, (-CO-NHR<sup>185</sup>, -CO-NR<sup>186</sup>R<sup>187</sup>), an **amido** group (-HN-CO-R<sup>188</sup>), a **sulfonic acid** group (-SO<sub>3</sub>H), a **sulfonamide** group (-SO<sub>2</sub>-NH<sub>2</sub>), a N-substituted or N,N-disubstituted **sulfonamide** group (-SO<sub>2</sub>-NHR<sup>189</sup>, -SO<sub>2</sub>-NR<sup>190</sup>R<sup>191</sup>), an **amidosulfone** group

(-NH-SO<sub>2</sub>-R<sup>192</sup>), a **sulfone** group (-SO<sub>2</sub>-R<sup>193</sup>), a **phosphoric acid** group (-OP(=O)(OH)<sub>2</sub>), a **phosphoric acid ester** group (-OP(=O)(OR<sup>194</sup>)(OR<sup>195</sup>)), a **phosphonic acid** group (-P(=O)(OH)<sub>2</sub>), an **phosphonic acid ester** group (-P(=O)(OR<sup>196</sup>)(OR<sup>197</sup>)), a **halogen atom**, a **trifluormethyl** group (-CF<sub>3</sub>), a **thiol** group (-SH); a **thioether** group (-S-R<sup>198</sup>), a **hydroxy** group (-OH); an **alkoxy** group (-O-R<sup>199</sup>), a **tetrazole** group, an **amino** group (-NH<sub>2</sub>), or a **N-substituted** or **N,N-disubstituted amino** group (-NHR<sup>200</sup>; -NR<sup>201</sup>R<sup>202</sup>); and

- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the pairs R<sup>186</sup>/R<sup>187</sup>, R<sup>190</sup>/R<sup>191</sup>, R<sup>194</sup>/R<sup>195</sup>, R<sup>196</sup>/R<sup>197</sup> and R<sup>201</sup>/R<sup>202</sup> independently of each other, may form a part of a **ring**; and
- wherein the substituents R<sup>180</sup>, R<sup>181</sup>, R<sup>182</sup>, R<sup>183</sup>, R<sup>184</sup>, R<sup>185</sup>, R<sup>186</sup>, R<sup>187</sup>, R<sup>188</sup>, R<sup>189</sup>, R<sup>190</sup>, R<sup>191</sup>, R<sup>192</sup>, R<sup>193</sup>, R<sup>194</sup>, R<sup>195</sup>, R<sup>196</sup>, R<sup>197</sup>, R<sup>198</sup>, R<sup>199</sup>, R<sup>200</sup>, R<sup>201</sup>, and R<sup>202</sup>, independently of each other are a **hydrogen** atom (-H), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

or wherein the group **PM**

has the formula (IV)



- wherein  $R^{211}$  and  $R^{212}$ , independently of each other, are
- a **hydrogen** atom (-H); or an  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkenyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkinyl**,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  **cycloalkyl**,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  **cycloalkenyl**, **aryl**, **heteroaryl** or an **amino** group ( $-NH_2$ ), or a N-substituted or N,N-disubstituted **amino** group ( $-NHR^{240}$ ;  $-NR^{241}R^{242}$ ); and
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the pairs  $R^{226}/R^{227}$ ,  $R^{230}/R^{231}$ ,  $R^{234}/R^{235}$ ,  $R^{236}/R^{237}$  and  $R^{241}/R^{242}$ , independently of each other, may form a part of a **ring**; and
  - wherein the substituents  $R^{220}$ ,  $R^{221}$ ,  $R^{222}$ ,  $R^{223}$ ,  $R^{224}$ ,  $R^{225}$ ,  $R^{226}$ ,  $R^{227}$ ,  $R^{228}$ ,  $R^{229}$ ,  $R^{230}$ ,  $R^{231}$ ,  $R^{232}$ ,  $R^{233}$ ,  $R^{234}$ ,  $R^{235}$ ,  $R^{236}$ ,  $R^{237}$ ,  $R^{238}$ ,  $R^{239}$ ,  $R^{240}$ ,  $R^{241}$ , and  $R^{242}$ , independently of each other, are a **hydrogen** atom (-H), or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkyl**, **aryl**, **heteroaryl**, **amino**, **halo**, **carbonyl**,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkoxy**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkenoxy**, **phenoxy**, **benzyloxy**,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  **cycloalkyl**, **cyano**, **amido**, **thiol**, **trifluoromethyl**, or **hydroxy** group; and
- wherein  $A^3$  is
- a **hydrogen** atom (-H); or a **carbaldehyde** ( $-CHO$ ), a **ketone** group ( $-CO-R^{260}$ ), a **boronic acid** group ( $-B(OH)_2$ ), a **cyano** group ( $-C\equiv N$ ), a **carboxylic acid** group ( $-COOH$ ), a **carboxylic acid ester** group ( $-COOR^{261}$ ), a **carboxylic acid anhydride** group ( $-CO-O-CO-R^{262}$ ), a **hydroxamic acid** group ( $-CO-NH(OH)$ ), a N-substituted **hydroxamic acid** group ( $-CO-NR^{263}(OH)$ ), a O-substituted **hydroxamic acid** group ( $-CO-NH(OR^{264})$ ), a **carboxamide** group ( $-CO-NH_2$ ), a N-substituted or N,N-disubstituted **carboxylic acid amide** group, ( $-CO-NHR^{265}$ ;

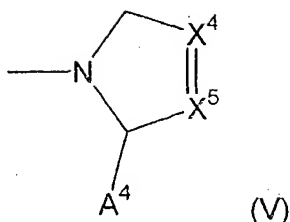
- CO-NR<sup>266</sup>R<sup>267</sup>), an **amido group** (-HN-CO-R<sup>268</sup>), a **sulfonic acid group** (-SO<sub>3</sub>H), a **sulfonamide group** (-SO<sub>2</sub>-NH<sub>2</sub>), a N-substituted or N,N-disubstituted **sulfonamide group** (-SO<sub>2</sub>-NHR<sup>269</sup>; -SO<sub>2</sub>-NR<sup>270</sup>R<sup>271</sup>), an **amidosulfone group** (-NH-SO<sub>2</sub>-R<sup>272</sup>), a **sulfone group** (-SO<sub>2</sub>-R<sup>273</sup>), a **phosphoric acid group** (-OP(=O)(OH)<sub>2</sub>), a **phosphoric acid ester group** (-OP(=O)(OR<sup>274</sup>)(OR<sup>275</sup>)), a **phosphonic acid group** (-P(=O)(OH)<sub>2</sub>), an **phosphonic acid ester group** (-P(=O)(OR<sup>276</sup>)(OR<sup>277</sup>)), a **halogen atom**, a **trifluormethyl group** (-CF<sub>3</sub>), a **thiol group** (-SH); a **thioether group** (-S-R<sup>278</sup>), a **hydroxy group** (-OH); an **alkoxy group** (-O-R<sup>279</sup>), a **tetrazole group**, an **amino group** (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted **amino group** (-NHR<sup>280</sup>; -NR<sup>281</sup>R<sup>282</sup>); and
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; and,
  - wherein optionally, the pairs R<sup>266</sup>/R<sup>267</sup>, R<sup>270</sup>/R<sup>271</sup>, R<sup>274</sup>/R<sup>275</sup>, R<sup>276</sup>/R<sup>277</sup> and R<sup>281</sup>/R<sup>282</sup>, independently of each other, may form a part of a **ring**; and
  - wherein the substituents R<sup>260</sup>, R<sup>261</sup>, R<sup>262</sup>, R<sup>263</sup>, R<sup>264</sup>, R<sup>265</sup>, R<sup>266</sup>, R<sup>267</sup>, R<sup>268</sup>, R<sup>269</sup>, R<sup>270</sup>, R<sup>271</sup>, R<sup>272</sup>, R<sup>273</sup>, R<sup>274</sup>, R<sup>275</sup>, R<sup>276</sup>, R<sup>277</sup>, R<sup>278</sup>, R<sup>279</sup>, R<sup>280</sup>, R<sup>281</sup>, and R<sup>282</sup>, independently of each other are a **hydrogen atom** (-H), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl group**;

or wherein the group PM

has the formula (V)



130

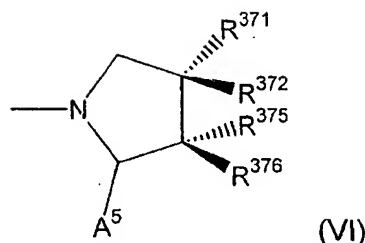


- wherein  $X^4$  is  $CR^{291}$  or N; and
- wherein  $X^5$  is  $CR^{292}$  or N; and
- wherein  $R^{291}$  and  $R^{292}$ , independently of each other, are
- a **hydrogen** atom (-H); or an  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkenyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkinyl**,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  **cycloalkyl**,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  **cycloalkenyl**, **aryl**, **heteroaryl** group, or an **amino** group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted **amino** group (-NHR<sup>320</sup>; -NR<sup>321</sup>R<sup>322</sup>); and
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the the pair  $R^{291}/R^{292}$ , if present, as well the pairs  $R^{306}/R^{307}$ ,  $R^{310}/R^{311}$ ,  $R^{314}/R^{315}$ ,  $R^{316}/R^{317}$  and  $R^{321}/R^{322}$ , independently of each other, may form a part of a **ring**; and
- wherein the substituents  $R^{300}$ ,  $R^{301}$ ,  $R^{302}$ ,  $R^{303}$ ,  $R^{304}$ ,  $R^{305}$ ,  $R^{306}$ ,  $R^{307}$ ,  $R^{308}$ ,  $R^{309}$ ,  $R^{310}$ ,  $R^{311}$ ,  $R^{312}$ ,  $R^{313}$ ,  $R^{314}$ ,  $R^{315}$ ,  $R^{316}$ ,  $R^{317}$ ,  $R^{318}$ ,  $R^{319}$ ,  $R^{320}$ ,  $R^{321}$ , and  $R^{322}$ , independently of each other are a **hydrogen** atom (-H), or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkyl**, **aryl**, **heteroaryl**, **amino**, **halo**, **carbonyl**,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkoxy**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkenoxy**, **phenyloxy**, **benzyloxy**,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  **cycloalkyl**, **cyano**, **amido**, **thiol**, **trifluoromethyl**, or **hydroxy** group; and

- wherein A<sup>4</sup> is
- a hydrogen atom (-H); or a **carbalddehyde** (-CHO), a **ketone** group (-CO-R<sup>340</sup>), a **boronic acid** group (-B(OH)<sub>2</sub>), a **cyano** group (-C≡N), a **carboxylic acid** group (-COOH), a **carboxylic acid ester** group (-COOR<sup>341</sup>), a **carboxylic acid anhydride** group (-CO-O-CO-R<sup>342</sup>), a **hydroxamic acid** group (-CO-NH(OH)), a **N-substituted hydroxamic acid** group (-CO-NR<sup>343</sup>(OH)), a **O-substituted hydroxamic acid** group (-CO-NH(OR<sup>344</sup>)), a **carboxamide** group (-CO-NH<sub>2</sub>), a **N-substituted or N,N-disubstituted carboxylic acid amide** group, (-CO-NHR<sup>345</sup>; -CO-NR<sup>346</sup>R<sup>347</sup>), an **amido** group (-HN-CO-R<sup>348</sup>), a **sulfonic acid** group (-SO<sub>3</sub>H), a **sulfonamide** group (-SO<sub>2</sub>-NH<sub>2</sub>), a **N-substituted or N,N-disubstituted sulfonamide** group (-SO<sub>2</sub>-NHR<sup>349</sup>; -SO<sub>2</sub>-NR<sup>350</sup>R<sup>351</sup>), an **amidosulfone** group (-NH-SO<sub>2</sub>-R<sup>352</sup>), a **sulfone** group (-SO<sub>2</sub>-R<sup>353</sup>), a **phosphoric acid** group (-OP(=O)(OH)<sub>2</sub>), a **phosphoric acid ester** group (-OP(=O)(OR<sup>354</sup>)(OR<sup>355</sup>)), a **phosphonic acid** group (-P(=O)(OH)<sub>2</sub>), an **phosphonic acid ester** group (-P(=O)(OR<sup>356</sup>)(OR<sup>357</sup>)), a **halogen atom**, a **trifluormethyl** group (-CF<sub>3</sub>), a **thiol** group (-SH); a **thioether** group (-S-R<sup>358</sup>), a **hydroxy** group (-OH); an **alkoxy** group (-O-R<sup>359</sup>), a **tetrazole** group, an **amino** group (-NH<sub>2</sub>), or a **N-substituted or N,N-disubstituted amino** group (-NHR<sup>360</sup>; -NR<sup>361</sup>R<sup>362</sup>); and
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the pairs R<sup>346</sup>/R<sup>347</sup>, R<sup>350</sup>/R<sup>351</sup>, R<sup>354</sup>/R<sup>355</sup>, R<sup>356</sup>/R<sup>357</sup> and R<sup>361</sup>/R<sup>362</sup>, independently of each other, may form a part of a **ring**; and
- wherein the substituents R<sup>340</sup>, R<sup>341</sup>, R<sup>342</sup>, R<sup>343</sup>, R<sup>344</sup>, R<sup>345</sup>, R<sup>346</sup>, R<sup>347</sup>, R<sup>348</sup>, R<sup>349</sup>, R<sup>350</sup>, R<sup>351</sup>, R<sup>352</sup>, R<sup>353</sup>, R<sup>354</sup>, R<sup>355</sup>, R<sup>356</sup>, R<sup>357</sup>, R<sup>358</sup>, R<sup>359</sup>, R<sup>360</sup>, R<sup>361</sup>, and R<sup>362</sup>, independently of each other are a **hydrogen** atom (-H), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

or wherein the group PM

has the formula (VI)



- wherein  $R^{371}$ ,  $R^{372}$ ,  $R^{375}$  and  $R^{376}$ , independently of each other, a **hydrogen atom** (-H); or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkenyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkinyl**,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  **cycloalkyl**,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  **cycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group or, a **carbaldehyde** (-CHO), a **ketone** group (-CO- $R^{380}$ ), a **boronic acid** group (-B(OH)<sub>2</sub>), a **cyano** group (-C≡N), a **carboxylic acid** group (-COOH), a **carboxylic acid ester** group (-COOR<sup>381</sup>), a **halogen atom**, a **trifluormethyl** group (-CF<sub>3</sub>), a **thiol** group (-SH); a **thioether** group (-S- $R^{398}$ ), a **hydroxy** group (-OH); an **alkoxy** group (-O- $R^{399}$ ), a **tetrazole** group, an **amino** group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted **amino** group (-NHR<sup>400</sup>; -NR<sup>401</sup>R<sup>402</sup>); and
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, any **two of the groups**  $R^{371}$ ,  $R^{372}$ ,  $R^{375}$ , and  $R^{376}$ , as well as the pairs  $R^{386}/R^{387}$ ,  $R^{390}/R^{391}$ ,  $R^{394}/R^{395}$ ,  $R^{396}/R^{397}$  and  $R^{401}/R^{402}$ , independently of each other, may form a part of a **ring**; and

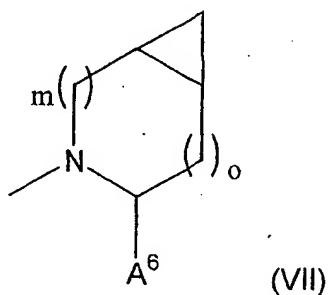
- wherein the substituents  $R^{380}$ ,  $R^{381}$ ,  $R^{382}$ ,  $R^{383}$ ,  $R^{384}$ ,  $R^{385}$ ,  $R^{386}$ ,  $R^{387}$ ,  $R^{388}$ ,  $R^{389}$ ,  $R^{390}$ ,  $R^{391}$ ,  $R^{392}$ ,  $R^{393}$ ,  $R^{394}$ ,  $R^{395}$ ,  $R^{396}$ ,  $R^{397}$ ,  $R^{398}$ ,  $R^{399}$ ,  $R^{400}$ ,  $R^{401}$ , and  $R^{402}$ , independently of each other are a **hydrogen** atom (-H), or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkyl**, **aryl**, **heteroaryl**, **amino**, **halo**, **carbonyl**,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkoxy**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkenoxy**, **phenyloxy**, **benzyloxy**,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  **cycloalkyl**, **cyano**, **amido**, **thiol**, **trifluoromethyl**, or **hydroxy** group; and
- alternatively; the two groups  $R^{371}$  and  $R^{372}$  can be together an **oxo** (=O) or **hydroxyimino** (=N-OH) group; and
- alternatively; the two groups  $R^{375}$  and  $R^{376}$  can be together an **oxo** (=O) or **hydroxyimino** (=N-OH) group; and
- wherein  $A^5$  is
- a **hydrogen** atom (-H); or a **carbaldehyde** (-CHO), a **ketone** group (-CO- $R^{420}$ ), a **boronic acid** group (-B(OH)<sub>2</sub>), a **cyano** group (-C≡N), a **carboxylic acid** group (-COOH), a **carboxylic acid ester** group (-COOR<sup>421</sup>), a **carboxylic acid anhydride** group (-CO-O-CO- $R^{422}$ ), a **hydroxamic acid** group (-CO-NH(OH)), a **N-substituted hydroxamic acid** group (-CO-NR<sup>423</sup>(OH)), a **O-substituted hydroxamic acid** group (-CO-NH(OR<sup>424</sup>)), a **carboxamide** group (-CO-NH<sub>2</sub>), a **N-substituted or N,N-disubstituted carboxylic acid amide** group, (-CO-NHR<sup>425</sup>; -CO-NR<sup>426</sup>R<sup>427</sup>), an **amido** group (-HN-CO- $R^{428}$ ), a **sulfonic acid** group (-SO<sub>3</sub>H), a **sulfonamide** group (-SO<sub>2</sub>-NH<sub>2</sub>), a **N-substituted or N,N-disubstituted sulfonamide** group (-SO<sub>2</sub>-NHR<sup>429</sup>; -SO<sub>2</sub>-NR<sup>430</sup>R<sup>431</sup>), an **amidosulfone** group (-NH-SO<sub>2</sub>- $R^{432}$ ), a **sulfone** group (-SO<sub>2</sub>- $R^{433}$ ), a **phosphoric acid** group (-OP(=O)(OH)<sub>2</sub>), a **phosphoric acid ester** group (-OP(=O)(OR<sup>434</sup>)(OR<sup>435</sup>)), a **phosphonic acid** group (-P(=O)(OH)<sub>2</sub>), an **phosphonic acid ester** group (-P(=O)(OR<sup>436</sup>)(OR<sup>437</sup>)), a **halogen atom**, a **trifluormethyl** group (-CF<sub>3</sub>), a **thiol** group (-SH); a **thioether** group (-S- $R^{438}$ ), a **hydroxy** group (-OH); an **alkoxy**

group ( $-O-R^{439}$ ), a **tetrazole** group, an **amino** group ( $-NH_2$ ), or a N-substituted or N,N-disubstituted **amino** group ( $-NHR^{440}$ ;  $-NR^{441}R^{442}$ ); and

- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the pairs  $R^{426}/R^{427}$ ,  $R^{430}/R^{431}$ ,  $R^{434}/R^{435}$ ,  $R^{436}/R^{437}$  and  $R^{441}/R^{442}$ , independently of each other, may form a part of a **ring**; and
- wherein the substituents  $R^{420}$ ,  $R^{421}$ ,  $R^{422}$ ,  $R^{423}$ ,  $R^{424}$ ,  $R^{425}$ ,  $R^{426}$ ,  $R^{427}$ ,  $R^{428}$ ,  $R^{429}$ ,  $R^{430}$ ,  $R^{431}$ ,  $R^{432}$ ,  $R^{433}$ ,  $R^{434}$ ,  $R^{435}$ ,  $R^{436}$ ,  $R^{437}$ ,  $R^{438}$ ,  $R^{439}$ ,  $R^{440}$ ,  $R^{441}$ , and  $R^{442}$ , independently of each other are a **hydrogen** atom ( $-H$ ), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

or wherein the group PM

has the formula (VII)

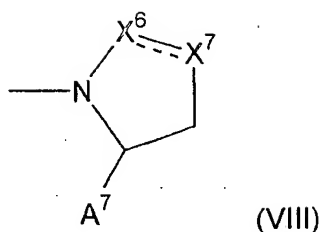


- wherein m is equal to 1 or 2, and o is equal to 1 or 2, and m or o can be 0;

- wherein  $A^6$  is a **hydrogen atom** (-H); or a **carbaldehyde** (-CHO), a **ketone group** (-CO-R<sup>460</sup>), a **boronic acid group** (-B(OH)<sub>2</sub>), a **cyano group** (-C≡N), a **carboxylic acid group** (-COOH), a **carboxylic acid ester group** (-COOR<sup>461</sup>), a **carboxylic acid anhydride group** (-CO-O-CO-R<sup>462</sup>), a **hydroxamic acid group** (-CO-NH(OH)), a N-substituted **hydroxamic acid group** (-CO-NR<sup>463</sup>(OH)), a O-substituted **hydroxamic acid group** (-CO-NH(OR<sup>464</sup>)), a **carboxamide group** (-CO-NH<sub>2</sub>), a N-substituted or N,N-disubstituted **carboxylic acid amide group**, (-CO-NHR<sup>465</sup>; -CO-NR<sup>466</sup>R<sup>467</sup>), an **amido group** (-HN-CO-R<sup>468</sup>), a **sulfonic acid group** (-SO<sub>3</sub>H), a **sulfonamide group** (-SO<sub>2</sub>-NH<sub>2</sub>), a N-substituted or N,N-disubstituted **sulfonamide group** (-SO<sub>2</sub>-NHR<sup>469</sup>; -SO<sub>2</sub>-NR<sup>470</sup>R<sup>471</sup>), an **amidosulfone group** (-NH-SO<sub>2</sub>-R<sup>472</sup>), a **sulfone group** (-SO<sub>2</sub>-R<sup>473</sup>), a **phosphoric acid group** (-OP(=O)(OH)<sub>2</sub>), a **phosphoric acid ester group** (-OP(=O)(OR<sup>474</sup>)(OR<sup>475</sup>)), a **phosphonic acid group** (-P(=O)(OH)<sub>2</sub>), an **phosphonic acid ester group** (-P(=O)(OR<sup>476</sup>)(OR<sup>477</sup>)), a **halogen atom**, a **trifluormethyl group** (-CF<sub>3</sub>), a **thiol group** (-SH); a **thioether group** (-S-R<sup>478</sup>), a **hydroxy group** (-OH); an **alkoxy group** (-O-R<sup>479</sup>), a **tetrazole group**, an **amino group** (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted **amino group** (-NHR<sup>480</sup>; -NR<sup>481</sup>R<sup>482</sup>);
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; and,
- wherein optionally, the pairs R<sup>466</sup>/R<sup>467</sup>, R<sup>470</sup>/R<sup>471</sup>, R<sup>474</sup>/R<sup>475</sup>, R<sup>476</sup>/R<sup>477</sup> and R<sup>481</sup>/R<sup>482</sup>, independently of each other, may form a part of a **ring**; and
- wherein the substituents R<sup>460</sup>, R<sup>461</sup>, R<sup>462</sup>, R<sup>463</sup>, R<sup>464</sup>, R<sup>465</sup>, R<sup>466</sup>, R<sup>467</sup>, R<sup>468</sup>, R<sup>469</sup>, R<sup>470</sup>, R<sup>471</sup>, R<sup>472</sup>, R<sup>473</sup>, R<sup>474</sup>, R<sup>475</sup>, R<sup>476</sup>, R<sup>477</sup>, R<sup>478</sup>, R<sup>479</sup>, R<sup>480</sup>, R<sup>481</sup>, and R<sup>482</sup>, independently of each other are a **hydrogen atom** (-H), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl group**;

or wherein the group PM

has the formula (VIII)



- wherein  $X^6$  is selected from  $CR^{490}R^{491}$ , O, S or  $NR^{492}$ , when the bond between  $X^6$  and  $X^7$  is a single bond; and
- wherein  $X^7$  is selected from  $CR^{493}R^{494}$ , O, S, or  $NR^{495}$ , when the bond between  $X^6$  and  $X^7$  is a single bond;
- **or alternatively,**
- wherein  $X^6$  is selected from  $CR^{496}$  or N, when the bond between  $X^6$  and  $X^7$  is a double bond; and
- wherein  $X^7$  is selected from  $CR^{497}$  or N, when the bond between  $X^6$  and  $X^7$  is a double bond; and
- wherein  $R^{490}$ ,  $R^{491}$ ,  $R^{492}$ ,  $R^{493}$ ,  $R^{494}$ ,  $R^{495}$ ,  $R^{496}$ , and  $R^{497}$ , independently of each other, are a **hydrogen** atom (-H); or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkenyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkinyl**,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  **cycloalkyl**,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  **cycloalkenyl**, **heteroalkyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group or, a **tetrazole** group, an **amino** group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted **amino** group (-NHR<sup>520</sup>; -NR<sup>521</sup>R<sup>522</sup>); and

- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, any two the groups  $R^{490}$ ,  $R^{491}$ ,  $R^{492}$ ,  $R^{493}$ ,  $R^{494}$ ,  $R^{495}$ ,  $R^{496}$ , and  $R^{497}$ , if present, as well as the pairs  $R^{506}/R^{507}$ ,  $R^{510}/R^{511}$ ,  $R^{514}/R^{515}$ ,  $R^{516}/R^{517}$  and  $R^{521}/R^{522}$ , independently of each other, may form a part of a **ring**; and
- wherein the substituents  $R^{500}$ ,  $R^{501}$ ,  $R^{502}$ ,  $R^{503}$ ,  $R^{504}$ ,  $R^{505}$ ,  $R^{506}$ ,  $R^{507}$ ,  $R^{508}$ ,  $R^{509}$ ,  $R^{510}$ ,  $R^{511}$ ,  $R^{512}$ ,  $R^{513}$ ,  $R^{514}$ ,  $R^{515}$ ,  $R^{516}$ ,  $R^{517}$ ,  $R^{518}$ ,  $R^{519}$ ,  $R^{520}$ ,  $R^{521}$ , and  $R^{522}$ , independently of each other are a **hydrogen atom (-H)**, or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group; and
- wherein  $A^7$  is
- a **hydrogen atom (-H)**; or a **carbaldehyde (-CHO)**, a **ketone group (-CO- $R^{540}$ )**, a **boronic acid group (-B(OH)<sub>2</sub>)**, a **cyano group (-C≡N)**, a **carboxylic acid group (-COOH)**, a **carboxylic acid ester group (-COOR<sup>541</sup>)**, a **carboxylic acid anhydride group (-CO-O-CO- $R^{542}$ )**, a **hydroxamic acid group (-CO-NH(OH))**, a **N-substituted hydroxamic acid group (-CO-NR<sup>543</sup>(OH))**, a **O-substituted hydroxamic acid group (-CO-NH(OR<sup>544</sup>))**, a **carboxamide group (-CO-NH<sub>2</sub>)**, a **N-substituted or N,N-disubstituted carboxylic acid amide group, (-CO-NHR<sup>545</sup>; -CO-NR<sup>546</sup>R<sup>547</sup>)**, an **amido group (-HN-CO- $R^{548}$ )**, a **sulfonic acid group (-SO<sub>3</sub>H)**, a **sulfonamide group (-SO<sub>2</sub>-NH<sub>2</sub>)**, a **N-substituted or N,N-disubstituted sulfonamide group (-SO<sub>2</sub>-NHR<sup>549</sup>; -SO<sub>2</sub>-NR<sup>550</sup>R<sup>551</sup>)**, an **amidosulfone group (-NH-SO<sub>2</sub>-R<sup>552</sup>)**, a **sulfone group (-SO<sub>2</sub>-R<sup>553</sup>)**, a **phosphoric acid group (-OP(=O)(OH)<sub>2</sub>)**, a **phosphoric acid ester group (-OP(=O)(OR<sup>554</sup>)(OR<sup>555</sup>))**, a **phosphonic acid group (-P(=O)(OH)<sub>2</sub>)**, an **phosphonic acid ester group (-P(=O)(OR<sup>556</sup>)(OR<sup>557</sup>))**, a **halogen atom**, a **trifluormethyl group (-CF<sub>3</sub>)**, a **thiol group (-SH)**; a **thioether group (-S-R<sup>558</sup>)**, a **hydroxy group (-OH)**; an **alkoxy**

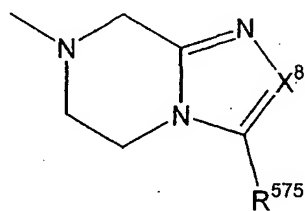


group ( $-O-R^{559}$ ), a **tetrazole** group, an **amino** group ( $-NH_2$ ), or a N-substituted or N,N-disubstituted **amino** group ( $-NHR^{560}$ ,  $-NR^{561}R^{562}$ ); and

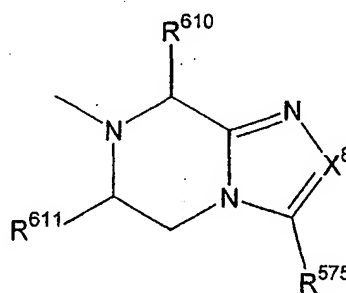
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; and,
- wherein optionally, the pairs  $R^{546}/R^{547}$ ,  $R^{550}/R^{551}$ ,  $R^{554}/R^{555}$ ,  $R^{556}/R^{557}$  and  $R^{561}/R^{562}$ , independently of each other, may form a part of a **ring**; and
- wherein the substituents  $R^{540}$ ,  $R^{541}$ ,  $R^{542}$ ,  $R^{543}$ ,  $R^{544}$ ,  $R^{545}$ ,  $R^{546}$ ,  $R^{547}$ ,  $R^{548}$ ,  $R^{549}$ ,  $R^{550}$ ,  $R^{551}$ ,  $R^{552}$ ,  $R^{553}$ ,  $R^{554}$ ,  $R^{555}$ ,  $R^{556}$ ,  $R^{557}$ ,  $R^{558}$ ,  $R^{559}$ ,  $R^{560}$ ,  $R^{561}$ , and  $R^{562}$ , independently of each other are a **hydrogen** atom ( $-H$ ), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

or wherein the group **PM**

has the formula (IX) or (IXa)



(IX)



(IXa)

- wherein  $X^8$  is N or  $CR^{570}$ ; and
- wherein  $R^{570}$ ,  $R^{575}$ ,  $R^{610}$  and  $R^{611}$  independently of each other, are

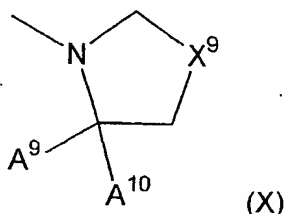
a **hydrogen** atom (-H); or an C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub> and C<sub>9</sub> branched or straight chain **alkyl**, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub> and C<sub>9</sub> branched or straight chain **alkenyl**, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub> and C<sub>9</sub> branched or straight chain **alkinyl**, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub> and C<sub>9</sub> **cycloalkyl**, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub> and C<sub>9</sub> **cycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **aryl-heteroalkyl** group or, a **carbaldehyde** (-CHO), a **ketone** group (-CO-R<sup>580</sup>), a **boronic acid** group (-B(OH)<sub>2</sub>), a **cyano** group (-C≡N), a **carboxylic acid** group (-COOH), a **carboxylic acid ester** group (-COOR<sup>581</sup>), a **carboxylic acid anhydride** group (-CO-O-CO-R<sup>582</sup>), a **hydroxamic acid** group (-CO-NH(OH)), a N-substituted **hydroxamic acid** group (-CO-NR<sup>583</sup>(OH)), a O-substituted **hydroxamic acid** group (-CO-NH(OR<sup>584</sup>)), a **carboxamide** group (-CO-NH<sub>2</sub>), a N-substituted or N,N-disubstituted **carboxylic acid amide** group, (-CO-NHR<sup>585</sup>; -CO-NR<sup>586</sup>R<sup>587</sup>), an **amido** group (-HN-CO-R<sup>588</sup>), a **sulfonic acid** group (-SO<sub>3</sub>H), a **sulfonamide** group (-SO<sub>2</sub>-NH<sub>2</sub>), a N-substituted or N,N-disubstituted **sulfonamide** group (-SO<sub>2</sub>-NHR<sup>589</sup>; -SO<sub>2</sub>-NR<sup>590</sup>R<sup>591</sup>), an **amidosulfone** group (-NH-SO<sub>2</sub>-R<sup>592</sup>), a **sulfone** group (-SO<sub>2</sub>-R<sup>593</sup>), a **phosphoric acid** group (-OP(=O)(OH)<sub>2</sub>), a **phosphoric acid ester** group (-OP(=O)(OR<sup>594</sup>)(OR<sup>595</sup>)), a **phosphonic acid** group (-P(=O)(OH)<sub>2</sub>), an **phosphonic acid ester** group (-P(=O)(OR<sup>596</sup>)(OR<sup>597</sup>)), a **halogen atom**, a **trifluormethyl** group (-CF<sub>3</sub>), a **thiol** group (-SH); a **thioether** group (-S-R<sup>598</sup>), a **hydroxy** group (-OH); an **alkoxy** group (-O-R<sup>599</sup>), a **tetrazole** group, an **amino** group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted **amino** group (-NHR<sup>600</sup>; -NR<sup>601</sup>R<sup>602</sup>);

- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; and,
- wherein optionally, the pairs R<sup>570</sup>/R<sup>575</sup>, if present, as well as the pairs R<sup>586</sup>/R<sup>587</sup>, R<sup>590</sup>/R<sup>591</sup>, R<sup>594</sup>/R<sup>595</sup>, R<sup>596</sup>/R<sup>597</sup> and R<sup>601</sup>/R<sup>602</sup>, independently of each other, may form a part of a **ring**; and
- wherein the substituents R<sup>580</sup>, R<sup>581</sup>, R<sup>582</sup>, R<sup>583</sup>, R<sup>584</sup>, R<sup>585</sup>, R<sup>586</sup>, R<sup>587</sup>, R<sup>588</sup>, R<sup>589</sup>, R<sup>590</sup>, R<sup>591</sup>, R<sup>592</sup>, R<sup>593</sup>, R<sup>594</sup>, R<sup>595</sup>, R<sup>596</sup>, R<sup>597</sup>, R<sup>598</sup>, R<sup>599</sup>, R<sup>600</sup>, R<sup>601</sup>, and

$R^{602}$ , independently of each other are a **hydrogen** atom (-H), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

or wherein the group PM

has the formula (X)



- wherein the groups  $X^9$  is  $CR^{900}R^{901}$ , S, SO, SO<sub>2</sub> or  $NR^{902}$ 
  - wherein  $R^{900}$ ,  $R^{901}$  and  $R^{902}$ , are, independently of each other, selected from hydrogen, fluorine, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens, or -C(=O)NR<sup>910</sup>R<sup>911</sup>.
- wherein  $A^9$  and  $A^{10}$  are, independently of each other, selected from hydrogen, cyano, -C(=O)NR<sup>912</sup>R<sup>913</sup>, or C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein

- $R^{910}$  and  $R^{912}$ , are, independently of each other, selected from hydrogen, or C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens; and

- $R^{911}$  and  $R^{913}$ , are, independently of each other, selected from the group consisting of
  - (1) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5, substituents independently selected from halogen and  $R^{920}$ ;
  - (2)  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6 or 7 substituents independently selected from (a) 0, 1, 2, 3, 4, or 5 halogens, and (b) 0, 1, 2 substituents selected from the group consisting of
    - (a) hydroxy,
    - (b)  $-COOH$ ,
    - (c)  $-COO(C_1, C_2, C_3, C_4, C_5$  or  $C_6$  alkyl), i.e. ester,
    - (d) phenyl,
    - (e) naphthyl,
    - (f)  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  cycloalkyl,
    - (g) a 5 - or 6 membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 heteroatoms independently selected from nitrogen , oxygen or sulfur;
    - (h) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (a) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (b) a benzene ring fused to a 5- or 6-membered heterocycle having 1, 2, or 3 hetero atoms;
- wherein said  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  cycloalkyl, phenyl, naphthyl, are optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from halogen and  $R^{920}$ , and said 5 or 6 membered heterocycle and said 8, 9 or 10 - membered bicyclic ring system are each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from from oxo, hydroxy, halogen, and  $R^{920}$ ; and

(3) C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, which is optionally substituted with 1, 2, or 3 groups independently selected from halogen, hydroxy, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein R<sup>920</sup> is selected from the group consisting of:

- (1) hydroxy;
- (2) cyano;
- (3) C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl optionally substituted with 1, 2, or 3 groups independently selected from halogen, hydroxy, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, wherein said -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl are linear or branched and are optionally substituted with 1, 2, 3, 4, 5 or 6 substituents selected from 1, 2, 3, 4, or 5 halogens, and 0 or 1 substituents selected from -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, -COOH, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl substituents being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;
- (4) C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub>, C<sub>9</sub> or C<sub>10</sub> alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6, or 7 substituents independently selected from 0, 1, 2, 3, 4, or 5 halogen atoms and 0, 1, or 2 groups selected from
  - (a) hydroxy;
  - (b) -COOH;
  - (c) -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, which may linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens;
  - (d) a 5- or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, optionally substituted with 1, 2, or 3

substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.;

(e) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (i) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (ii) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(f) -CONR<sup>925</sup>R<sup>925</sup>;

(g) -SO<sub>2</sub>NR<sup>925</sup>R<sup>925</sup>;

(h) -NR<sup>925</sup>-C(=O)R<sup>925</sup>

(i) -NR<sup>925</sup>-C(=O)NR<sup>925</sup>R<sup>925</sup>;

(j) -NR<sup>925</sup>COOR<sup>930</sup>

(k) -O-CO-R<sup>930</sup>

(l) -O-CO-NR<sup>925</sup>R<sup>925</sup>;

(m) -NR<sup>925</sup>SO<sub>2</sub>R<sup>930</sup>;

(n) -NR<sup>925</sup>R<sup>925</sup>;

(o) phenyl which is optionally substituted with 1, 2, 3, 4, or 5 group independently selected from halogen, hydroxy, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester being linear or branched and optionally substituted

with 1, 2, 3, 4, 5, or 6 substituents independently selected from 0 or 1

C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl and 0, 1, 2, 3, 4, or 5 halogens, and

(p) C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, which is optionally substituted with 1, 2, 3, 4, 5, or 6 halogens;

(5) OC<sub>1</sub>, OC<sub>2</sub>, OC<sub>3</sub>, OC<sub>4</sub>, OC<sub>5</sub>, OC<sub>6</sub>, OC<sub>7</sub>, OC<sub>8</sub>, OC<sub>9</sub> or OC<sub>10</sub> alkyl, which is linear or branched and is optionally substituted with 0, 1, 2, 3, 4, or 5 halogen atoms and 0, 1, or 2 substituents selected from

(a) hydroxy;

(b)-COOH;

(c) -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, which may be linear or branched and is optionally substituted with 1, 2, 3, 4 or 5 halogens;

(d) a 5 - or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.;

(e) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (i) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (ii) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(f) -CONR<sup>925</sup>R<sup>925</sup>;

- (g)  $-\text{SO}_2\text{NR}^{925}\text{R}^{925}$ ;
- (h)  $-\text{NR}^{925}-\text{C}(=\text{O})\text{R}^{925}$ ;
- (i)  $-\text{NR}^{925}-\text{C}(=\text{O})\text{NR}^{925}\text{R}^{925}$ ;
- (j)  $-\text{NR}^{925}\text{COOR}^{930}$
- (k)  $-\text{O}-\text{CO}-\text{R}^{930}$
- (l)  $-\text{O}-\text{CO}-\text{NR}^{925}\text{R}^{925}$ ;
- (m)  $-\text{NR}^{925}\text{SO}_2\text{R}^{930}$ ;
- (n)  $-\text{NR}^{925}\text{R}^{925}$ ;
- (o) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5 groups independently selected from halogen, hydroxy,  $\text{C}_1$ ,  $\text{C}_2$ ,  $\text{C}_3$ ,  $\text{C}_4$ ,  $\text{C}_5$  or  $\text{C}_6$  alkyl,  $-\text{OC}_1$ ,  $-\text{OC}_2$ ,  $-\text{OC}_3$ ,  $-\text{OC}_4$ ,  $-\text{OC}_5$  or  $-\text{OC}_6$  alkyl,  $-\text{COOH}$ ,  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester, said  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  alkyl,  $-\text{OC}_1$ ,  $-\text{OC}_2$ ,  $-\text{OC}_3$ ,  $-\text{OC}_4$ ,  $-\text{OC}_5$  or  $-\text{OC}_6$  alkyl,  $-\text{COOH}$ ,  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, 5, or 6 substituents independently selected from 0 or 1  $\text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  cycloalkyl and 0, 1, 2, 3, 4, or 5 halogens, and
- (p)  $\text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  cycloalkyl, which is optionally substituted with 1, 2, 3, 4, 5, or 6 halogens;
- (6)  $-\text{COOH}$ ;
- (7)  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester, which may be linear or branched and is optionally substituted with 1, 2, 3, 4, 5 halogens;
- (8) a 5 - or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, said heterocycle being optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen,  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5$  or  $-\text{OC}_6$  alkyl, said  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5$  or  $-\text{OC}_6$  alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.
- (9) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (a) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen,



oxygen or sulfur, or (b) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(10) -CONR<sup>925</sup>R<sup>925</sup>;

(11) -SO<sub>2</sub>NR<sup>925</sup>R<sup>925</sup>;

(12) -NR<sup>925</sup>-C(=O)R<sup>925</sup>

(13) -NR<sup>925</sup>-C(=O)NR<sup>925</sup>R<sup>925</sup>;

(14) -NR<sup>925</sup>COOR<sup>930</sup>

(15) -O-CO-R<sup>930</sup>

(16) -O-CO-NR<sup>925</sup>R<sup>925</sup>;

(17) -NR<sup>925</sup>SO<sub>2</sub>R<sup>930</sup>;

(18) -NR<sup>925</sup>R<sup>925</sup>;

(19) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5 group independently selected from halogen, hydroxy, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

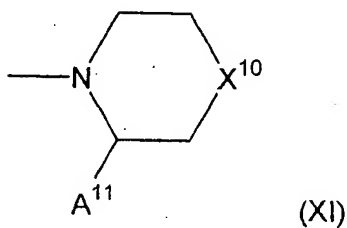
wherein R<sup>930</sup> is selected from the group consisting of phenyl, C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, and C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, wherein C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6, substituents independently selected from 0, 1, 2, 3, 4, or 5 halogens, 0 or 1 phenyl, wherein said optional phenyl substituent and said R<sup>930</sup>, when R<sup>930</sup> is phenyl or C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, are optionally substituted with 1, 2, 3, 4, or 5 substituents, independently selected from

halogen, OH, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, or C<sub>5</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, or -OC<sub>5</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, or C<sub>5</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, or -OC<sub>5</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.

wherein R<sup>925</sup> is selected from R<sup>930</sup> and hydrogen.

wherein the group PM

has the formula (XI)



- wherein the groups X<sup>10</sup> is CR<sup>1000</sup>R<sup>1001</sup>, S, SO, SO<sub>2</sub> or NR<sup>1002</sup>
  - wherein R<sup>1000</sup>, R<sup>1001</sup> and R<sup>1002</sup>, are, independently of each other, selected from hydrogen, fluorine, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens, or -C(=O)NR<sup>1010</sup>R<sup>1011</sup>.

and A<sup>11</sup> is selected from

hydrogen, cyano, -C(=O)NR<sup>1012</sup>R<sup>1013</sup>, or C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein

- R<sup>1010</sup> and R<sup>1012</sup>, are, independently of each other, selected from hydrogen, or C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens; and

- $R^{1011}$  and  $R^{1013}$ , are, independently of each other, selected from the group consisting of

(1) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5, substituents independently selected from halogen and  $R^{1020}$ ,

(2)  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6 or 7 substituents independently selected from (a) 0, 1, 2, 3, 4, or 5 halogens, and (b) 0, 1, 2 substituents selected from the group consisting of

- (a) hydroxy,
- (b)  $-COOH$ ,
- (c)  $-COO(C_1, C_2, C_3, C_4, C_5 \text{ or } C_6 \text{ alkyl})$ , i.e. ester,
- (d) phenyl,
- (e) naphthyl,
- (f)  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  cycloalkyl,
- (g) a 5- or 6 membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur;
- (h) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (a) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (b) a benzene ring fused to a 5- or 6-membered heterocycle having 1, 2, or 3 hetero atoms;

- wherein said  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  cycloalkyl, phenyl, naphthyl, are optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from halogen and  $R^{1020}$ , and said 5 or 6 membered heterocycle and said 8, 9 or 10 - membered bicyclic ring system are each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, and  $R^{1020}$ ; and

(3) C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, which is optionally substituted with 1, 2, or 3 groups independently selected from halogen, hydroxy, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein R<sup>1020</sup> is selected from the group consisting of:

- (1) hydroxy;
- (2) cyano;
- (3) C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl optionally substituted with 1, 2, or 3 groups independently selected from halogen, hydroxy, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, wherein said -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl are linear or branched and are optionally substituted with 1, 2, 3, 4, 5 or 6 substituents selected from 1, 2, 3, 4, or 5 halogens, and 0 or 1 substituents selected from -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, -COOH, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl substituents being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;
- (4) C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub>, C<sub>9</sub> or C<sub>10</sub> alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6, or 7 substituents independently selected from 0, 1, 2, 3, 4, or 5 halogen atoms and 0, 1, or 2 groups selected from
  - (a) hydroxy;
  - (b) -COOH;
  - (c) -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, which may linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens;
  - (d) a 5 - or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, optionally substituted with 1, 2, or 3

substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.;

(e) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (i) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (ii) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(f) -CONR<sup>1025</sup>R<sup>1025</sup>;

(g) -SO<sub>2</sub>NR<sup>1025</sup>R<sup>1025</sup>;

(h) -NR<sup>1025</sup>-C(=O)R<sup>1025</sup>

(i) -NR<sup>1025</sup>-C(=O)NR<sup>1025</sup>R<sup>1025</sup>;

(j) -NR<sup>1025</sup>COOR<sup>1030</sup>

(k) -O-CO-R<sup>1030</sup>

(l) -O-CO-NR<sup>1025</sup>R<sup>1025</sup>;

(m) -NR<sup>1025</sup>SO<sub>2</sub>R<sup>1030</sup>;

(n) -NR<sup>1025</sup>R<sup>1025</sup>;

(o) phenyl which is optionally substituted with 1, 2, 3, 4, or 5 group independently selected from halogen, hydroxy, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester being linear or branched and optionally substituted

with 1, 2, 3, 4, 5, or 6 substituents independently selected from 0 or 1

C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl and 0, 1, 2, 3, 4, or 5 halogens, and

(p) C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl, which is optionally substituted with 1, 2, 3, 4, 5, or 6 halogens;

(5) OC<sub>1</sub>, OC<sub>2</sub>, OC<sub>3</sub>, OC<sub>4</sub>, OC<sub>5</sub>, OC<sub>6</sub>, OC<sub>7</sub>, OC<sub>8</sub>, OC<sub>9</sub> or OC<sub>10</sub> alkyl, which is linear or branched and is optionally substituted with 0, 1, 2, 3, 4, or 5 halogen atoms and 0, 1, or 2 substituents selected from

(a) hydroxy;

(b)-COOH;

(c) -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, which may be linear or branched and is optionally substituted with 1, 2, 3, 4 or 5 halogens;

(d) a 5- or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.;

(e) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (i) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (ii) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(f) -CONR<sup>1025</sup>R<sup>1025</sup>;

(g)  $-\text{SO}_2\text{NR}^{1025}\text{R}^{1025}$ ;

(h)  $-\text{NR}^{1025}-\text{C}(=\text{O})\text{R}^{1025}$

(i)  $-\text{NR}^{1025}-\text{C}(=\text{O})\text{NR}^{1025}\text{R}^{1025}$ ;

(j)  $-\text{NR}^{1025}\text{COOR}^{1030}$

(k)  $-\text{O}-\text{CO}-\text{R}^{1030}$

(l)  $-\text{O}-\text{CO}-\text{NR}^{1025}\text{R}^{1025}$ ;

(m)  $-\text{NR}^{1025}\text{SO}_2\text{R}^{1030}$ ;

(n)  $-\text{NR}^{1025}\text{R}^{1025}$ ;

(o) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5 groups independently selected from halogen, hydroxy,  $\text{C}_1$ ,  $\text{C}_2$ ,  $\text{C}_3$ ,  $\text{C}_4$ ,  $\text{C}_5$  or  $\text{C}_6$  alkyl,  $-\text{OC}_1$ ,  $-\text{OC}_2$ ,  $-\text{OC}_3$ ,  $-\text{OC}_4$ ,  $-\text{OC}_5$  or  $-\text{OC}_6$  alkyl,  $-\text{COOH}$ ,  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester, said  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  alkyl,  $-\text{OC}_1$ ,  $-\text{OC}_2$ ,  $-\text{OC}_3$ ,  $-\text{OC}_4$ ,  $-\text{OC}_5$  or  $-\text{OC}_6$  alkyl,  $-\text{COOH}$ ,  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, 5, or 6 substituents independently selected from 0 or 1  $\text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  cycloalkyl and 0, 1, 2, 3, 4, or 5 halogens, and

(p)  $\text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  cycloalkyl, which is optionally substituted with 1, 2, 3, 4, 5, or 6 halogens;

(6)  $-\text{COOH}$ ;

(7)  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester, which may be linear or branched and is optionally substituted with 1, 2, 3, 4, 5 halogens;

(8) a 5- or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, said heterocycle being optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen,  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5$  or  $-\text{OC}_6$  alkyl, said  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5$  or  $-\text{OC}_6$  alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.

(9) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (a) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen,

oxygen or sulfur, or (b) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(10) -CONR<sup>1025</sup>R<sup>1025</sup>;

(11) -SO<sub>2</sub>NR<sup>1025</sup>R<sup>1025</sup>;

(12) -NR<sup>1025</sup>-C(=O)R<sup>1025</sup>

(13) -NR<sup>1025</sup>-C(=O)NR<sup>1025</sup>R<sup>1025</sup>;

(14) -NR<sup>925</sup>COOR<sup>1030</sup>

(15) -O-CO-R<sup>1030</sup>

(16) -O-CO-NR<sup>1025</sup>R<sup>1025</sup>;

(17) -NR<sup>1025</sup>SO<sub>2</sub>R<sup>1030</sup>;

(18) -NR<sup>1025</sup>R<sup>1025</sup>;

(19) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5 group independently selected from halogen, hydroxy, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein R<sup>1030</sup> is selected from the group consisting of phenyl, C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, and C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, wherein C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6, substituents independently selected from 0, 1, 2, 3, 4, or 5 halogens, 0 or 1 phenyl, wherein said optional phenyl substituent and said R<sup>930</sup>, when R<sup>930</sup> is phenyl or C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, are optionally substituted with 1, 2, 3, 4, or 5 substituents, independently selected from

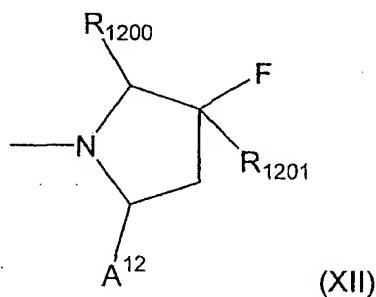


halogen, OH, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, or C<sub>5</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, or -OC<sub>5</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, or C<sub>5</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, or -OC<sub>5</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.

wherein R<sup>1025</sup> is selected from R<sup>1030</sup> and hydrogen.

or wherein the group PM

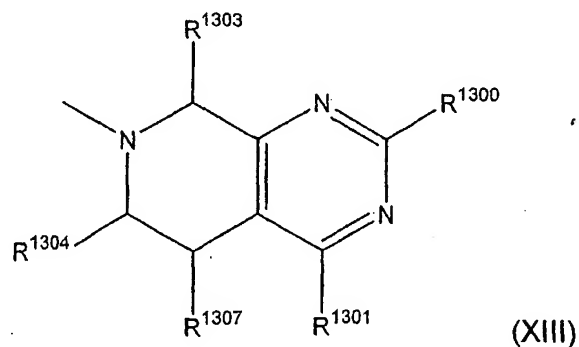
has the formula (XII)



- wherein the groups R<sup>1201</sup> is hydrogen or fluoro.
- wherein R<sup>1200</sup> and A<sup>12</sup> is selected from hydrogen and cyano, and the other is hydrogen.

or wherein the group PM

has the formula XIII:



wherein:

-  $R^{1300}$  and  $R^{1301}$  are independently selected from the group consisting of:

- (1) hydrogen,
- (2) CN,
- (3)  $C_{1-10}$ alkyl, which is linear or branched which is unsubstituted or substituted with:
  - a) halogen, or
  - b) phenyl, which is unsubstituted or substituted with 1 - 5 substituents independently selected from halogen, CN, OH,  $R^{1302}$ ,  $OR^{1302}$ ,  $NHSO_2R^{1302}$ ,  $N(C_{1-6}alkyl)SO_2R^{1302}$ ,  $SO_2R^{1302}$ ,  $SO_2NR^{1305}R^{1306}$ ,  $NR^{1305}R^{1306}$ ,  $CONR^{1305}R^{1306}$ ,  $CO_2H$ , and  $CO_2C_{1-6}alkyl$ , wherein the  $C_{1-6}alkyl$  is linear or branched,
- (4) phenyl which is unsubstituted or substituted with 1 - 5 substituents independently selected from halogen, CN, OH,  $R^{1302}$ ,  $OR^{1302}$ ,  $NHSO_2R^{1302}$ ,  $N(C_{1-6}alkyl)SO_2R^{1302}$ ,  $SO_2R^{1302}$ ,  $SO_2NR^{1305}R^{1306}$ ,  $NR^{1305}R^{1306}$ ,  $CONR^{1305}R^{1306}$ ,  $CO_2H$ , and  $CO_2C_{1-6}alkyl$ , wherein the  $C_{1-6}alkyl$  is linear or branched,
- (5) a 5- or 6-membered heterocyclic which may be saturated or unsaturated comprising 1 - 4 heteroatoms independently selected from N, S and O, the heterocycle being unsubstituted or substituted with 1 - 3 substituents independently selected from oxo, halogen,  $NO_2$ , CN, OH,  $R^{1302}$ ,  $OR^{1302}$ ,  $NHSO_2R^{1302}$ ,  $N(C_{1-6}alkyl)SO_2R^{1302}$ ,  $SO_2R^{1302}$ ,  $SO_2NR^{1305}R^{1306}$ ,  $NR^{1305}R^{1306}$ ,  $CONR^{1305}R^{1306}$ ,  $CO_2H$ , and  $CO_2C_{1-6}alkyl$ , wherein the  $C_{1-6}alkyl$  is linear or branched,
- (6)  $C_{3-6}$ cycloalkyl, which is optionally substituted with 1 - 5 substituents independently selected from halogen, OH,  $C_{1-6}alkyl$ , and  $OC_{1-6}alkyl$ , wherein the  $C_{1-6}alkyl$  and  $OC_{1-6}alkyl$  are linear or branched and optionally substituted with 1 - 5 halogens,
- (7) OH,
- (8)  $OR^{1302}$ , and
- (9)  $NR^{1305}R^{1306}$

-  $R^{1302}$  is  $C_{1-6}$ alkyl, which is linear or branched and which is unsubstituted or substituted with 1 – 5 groups independently selected from halogen,  $CO_2H$ , and  $CO_2C_{1-6}$ alkyl, wherein the  $C_{1-6}$ alkyl is linear or branched;

-  $R^{1303}$  is selected from the group consisting of:

(1) hydrogen,

(2)  $C_{1-10}$ alkyl, which is linear or branched and which is unsubstituted or substituted with one or more substituted selected from:

a) halogen,

b) hydroxy,

c) phenyl, which is unsubstituted or substituted with 1 – 5 substituents independently selected from halogen, OH,  $C_{1-6}$ alkyl, and  $OC_{1-6}$ alkyl, wherein the  $C_{1-6}$ alkyl is linear or branched and optionally substituted with 1 – 5 halogens,

d) naphthyl, wherein the naphthyl is optionally substituted with 1 – 5 substituents independently selected from halogen, OH,  $C_{1-6}$ alkyl, and  $OC_{1-6}$ alkyl, wherein the  $C_{1-6}$ alkyl is linear or branched and optionally substituted with 1 – 5 halogens,

h)  $CO_2H$ ,

i)  $CO_2C_{1-6}$ alkyl,

j)  $CONR^{1305}R^{1306}$ ,

(3) CN,

(4) phenyl which is unsubstituted or substituted with 1 – 5 substituents independently selected from  $C_{1-6}$ alkyl, and  $OC_{1-6}$ alkyl, hydroxy and halogen, wherein the  $C_{1-6}$ alkyl is linear or branched and optionally substituted with 1 – 5 halogens

(5) naphthyl which is unsubstituted or substituted with 1 – 5 substituents independently selected from  $C_{1-6}$ alkyl, and  $OC_{1-6}$ alkyl, hydroxy and halogen, wherein the  $C_{1-6}$ alkyl is linear or branched and optionally substituted with 1 – 5 halogens,

- (6)  $\text{CO}_2\text{H}$ ,
- (7)  $\text{CO}_2\text{C}_{1-6}\text{alkyl}$ ,
- (8)  $\text{CONR}^{1305}\text{R}^{1306}$ , and
- (9)  $\text{C}_{3-6}\text{cycloalkyl}$ , which is unsubstituted or substituted with 1 – 5 substituents independently selected from  $\text{C}_{1-6}\text{alkyl}$ , and  $\text{OC}_{1-6}\text{alkyl}$ , hydroxy and halogen, wherein the  $\text{C}_{1-6}\text{alkyl}$  is linear or branched and optionally substituted with 1 – 5 halogens

-  $\text{R}^{1305}$  and  $\text{R}^{1306}$  are independently selected from the group consisting of:

- (1) hydrogen,
- (2) phenyl, which is unsubstituted or substituted with substituents independently selected from halogen, OH,  $\text{C}_{1-6}\text{alkyl}$ , and  $\text{OC}_{1-6}\text{alkyl}$ , wherein the  $\text{C}_{1-6}\text{alkyl}$  is linear or branched and optionally substituted with 1 – 5 halogens,
- (3)  $\text{C}_{3-6}\text{cycloalkyl}$ , which is unsubstituted or substituted with 1 – 5 substituents independently selected from  $\text{C}_{1-6}\text{alkyl}$ , and  $\text{OC}_{1-6}\text{alkyl}$ , wherein the  $\text{C}_{1-6}\text{alkyl}$  is linear or branched and optionally substituted with 1 – 5 halogens,
- (4)  $\text{C}_{1-6}\text{alkyl}$ , which is linear or branched and which is unsubstituted or substituted with:

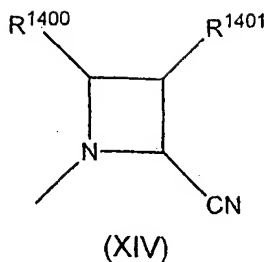
- a) halogen, or
- b) phenyl, which is unsubstituted or substituted with 1 – 5 substituents independently selected from halogen, OH,  $\text{C}_{1-6}\text{alkyl}$ , and  $\text{OC}_{1-6}\text{alkyl}$ , wherein the  $\text{C}_{1-6}\text{alkyl}$  is linear or branched and optionally substituted with 1 – 5 halogens,

or wherein  $\text{R}^{1305}$  and  $\text{R}^{1306}$  together with the nitrogen atom to which they are attached form a heterocyclic ring selected from azetidine, pyrrolidine, piperidine, piperazine, and morpholine wherein said heterocyclic ring is unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy,  $\text{C}_{1-6}\text{alkyl}$ , and  $\text{C}_{1-6}\text{alkoxy}$ , wherein alkyl and alkoxy are unsubstituted with one to five halogens;

-  $\text{R}^{1304}$  and  $\text{R}^{1307}$  are hydrogen;

or wherein the group PM

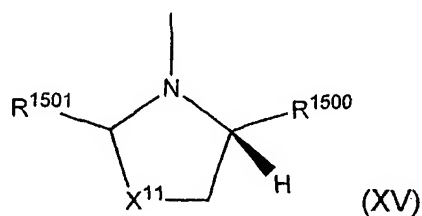
has the formula XIV:



- wherein R<sup>1400</sup> and R<sup>1401</sup>, independently of each other, are a **hydrogen** atom (-H); or halogen, cyano or ethynyl;

or wherein the group PM

has the formula XV:

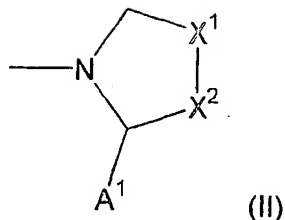


- wherein X<sup>11</sup> is CH<sub>2</sub>, CHF or CF<sub>2</sub>;
- wherein R<sup>1500</sup> is cyano;
- wherein R<sup>1501</sup> is selected from the group consisting of alkoxyalkyl, alkyl, alkylcarbonyl, alkenyl, alkynyl, allenyl, arylalkyl, cycloalkyl, cycloalkylalkyl, cyano, haloalkyl, haloalkenyl, heterocyclealkyl, and hydroxyalkyl;

Preferred are compounds as disclosed above

wherein the group PM

has the formula (II)



- wherein  $X^1$  is  $CR^{51}R^{52}$ , O, S, or  $NR^{53}$ ; and
- wherein  $X^2$  is  $CR^{54}R^{55}$ , O, S, or  $NR^{56}$ ; and

wherein  $R^{51}$ ,  $R^{52}$ ,  $R^{53}$ ,  $R^{54}$ ,  $R^{55}$ , and  $R^{56}$ , independently of each other, are

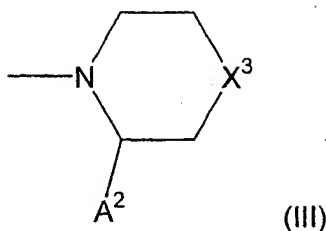
- a **hydrogen** atom (-H); or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , and  $C_5$  branched or straight chain **alkyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkenyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkinyl**,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ , and  $C_7$  **cycloalkyl**, **aryl**, **heteroaryl** group or, an **amino** group ( $-NH_2$ ), or a N-substituted or N,N-disubstituted **amino** group ( $-NHR^{80}$ ;  $-NR^{81}R^{82}$ ); and
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; and,
- wherein optionally, any **two of the groups**  $R^{51}$ ,  $R^{52}$ ,  $R^{53}$ ,  $R^{54}$ ,  $R^{55}$ , and  $R^{56}$ , if present, as well as the pairs  $R^{66}/R^{67}$ ,  $R^{70}/R^{71}$ ,  $R^{74}/R^{75}$ ,  $R^{76}/R^{77}$  and  $R^{81}/R^{82}$ , independently of each other, may form a part of a **ring**; and
- wherein the substituents  $R^{60}$ ,  $R^{61}$ ,  $R^{62}$ ,  $R^{63}$ ,  $R^{64}$ ,  $R^{65}$ ,  $R^{66}$ ,  $R^{67}$ ,  $R^{68}$ ,  $R^{69}$ ,  $R^{70}$ ,  $R^{71}$ ,  $R^{72}$ ,  $R^{73}$ ,  $R^{74}$ ,  $R^{75}$ ,  $R^{76}$ ,  $R^{77}$ ,  $R^{78}$ ,  $R^{79}$ ,  $R^{80}$ ,  $R^{81}$ , and  $R^{82}$ , independently of each other, are a **hydrogen** atom (-H), or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , and  $C_5$  branched or straight chain **alkyl**, **aryl**, **heteroaryl**, **amino**, **halo**, **carbonyl**,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkoxy**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  branched or straight chain **alkenoxy**, **phenyloxy**, **benzyloxy**,  $C_3$ ,  $C_4$ ,  $C_5$  **cycloalkyl**, **cyano**, **amido**, **thiol** **trifluoromethyl**, or **hydroxy** group; and

wherein A<sup>1</sup> is

- a hydrogen atom (-H) or a carbaldehyde (-CHO), a ketone group (-CO-R<sup>100</sup>), a boronic acid group (-B(OH)<sub>2</sub>), a cyano group (-C≡N), a carboxylic acid group (-COOH), a carboxylic acid ester group (-COOR<sup>101</sup>), a carboxylic acid anhydride group (-CO-O-CO-R<sup>102</sup>), a hydroxamic acid group (-CO-NH(OH)), a N-substituted hydroxamic acid group (-CO-NR<sup>103</sup>(OH)), a O-substituted hydroxamic acid group (-CO-NH(OR<sup>104</sup>)), a carboxamide group (-CO-NH<sub>2</sub>), a N-substituted or N,N-disubstituted carboxylic acid amide group, (-CO-NHR<sup>105</sup>, -CO-NR<sup>106</sup>R<sup>107</sup>), an amido group (-HN-CO-R<sup>108</sup>), a sulfonic acid group (-SO<sub>3</sub>H), a sulfonamide group (-SO<sub>2</sub>-NH<sub>2</sub>), a N-substituted or N,N-disubstituted sulfonamide group (-SO<sub>2</sub>-NHR<sup>109</sup>, -SO<sub>2</sub>-NR<sup>110</sup>R<sup>111</sup>), an amidosulfone group (-NH-SO<sub>2</sub>-R<sup>112</sup>), a sulfone group (-SO<sub>2</sub>-R<sup>113</sup>), a phosphoric acid group (-OP(=O)(OH)<sub>2</sub>), a phosphoric acid ester group (-OP(=O)(OR<sup>114</sup>)(OR<sup>115</sup>)), a phosphonic acid group (-P(=O)(OH)<sub>2</sub>), an phosphonic acid ester group (-P(=O)(OR<sup>116</sup>)(OR<sup>117</sup>)), a halogen atom, a trifluormethyl group (-CF<sub>3</sub>), a thiol group (-SH); a thioether group (-S-R<sup>118</sup>), a hydroxy group (-OH); an alkoxy group (-O-R<sup>119</sup>), a tetrazole group, an amino group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted amino group (-NHR<sup>120</sup>, -NR<sup>121</sup>R<sup>122</sup>); and wherein optionally, the pairs R<sup>106</sup>/R<sup>107</sup>, R<sup>110</sup>/R<sup>111</sup>, R<sup>114</sup>/R<sup>115</sup>, R<sup>116</sup>/R<sup>117</sup> and R<sup>121</sup>/R<sup>122</sup>, independently of each other, may form a part of a ring; and
- which, independently of each other, can be substituted with one or more substituents, which can be the same or different; and,
- wherein the substituents R<sup>100</sup>, R<sup>101</sup>, R<sup>102</sup>, R<sup>103</sup>, R<sup>104</sup>, R<sup>105</sup>, R<sup>106</sup>, R<sup>107</sup>, R<sup>108</sup>, R<sup>109</sup>, R<sup>110</sup>, R<sup>111</sup>, R<sup>112</sup>, R<sup>113</sup>, R<sup>114</sup>, R<sup>115</sup>, R<sup>116</sup>, R<sup>117</sup>, R<sup>118</sup>, R<sup>119</sup>, R<sup>120</sup>, R<sup>121</sup>, and R<sup>122</sup>, independently of each other, are a hydrogen atom (-H), or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group;

or wherein the group PM

has the formula (III)



- wherein  $X^3$  is  $CR^{131}R^{132}$ , O, S, or  $NR^{133}$ ; and
- wherein  $R^{131}$ ,  $R^{132}$ , and  $R^{133}$ , independently of each other, are
- a **hydrogen** atom (-H); or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , and  $C_5$  branched or straight chain **alkyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkenyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkinyl**,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ , and  $C_7$  **cycloalkyl**, **aryl**, **heteroaryl** group or, an **amino** group ( $-NH_2$ ), or a N-substituted or N,N-disubstituted **amino** group ( $-NHR^{160}$ ,  $-NR^{161}R^{162}$ ); and
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the **the pair**  $R^{131}/R^{132}$ , if present, as well the pairs  $R^{146}/R^{147}$ ,  $R^{150}/R^{151}$ ,  $R^{154}/R^{155}$ ,  $R^{156}/R^{157}$  and  $R^{161}/R^{162}$ , independently of each other, may form a part of a **ring**; and
- wherein the substituents  $R^{140}$ ,  $R^{141}$ ,  $R^{142}$ ,  $R^{143}$ ,  $R^{144}$ ,  $R^{145}$ ,  $R^{146}$ ,  $R^{147}$ ,  $R^{148}$ ,  $R^{149}$ ,  $R^{150}$ ,  $R^{151}$ ,  $R^{152}$ ,  $R^{153}$ ,  $R^{154}$ ,  $R^{155}$ ,  $R^{156}$ ,  $R^{157}$ ,  $R^{158}$ ,  $R^{159}$ ,  $R^{160}$ ,  $R^{161}$ , and  $R^{162}$ , independently of each other are a **hydrogen** atom (-H), or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , and  $C_5$  branched or straight chain **alkyl**, **aryl**, **heteroaryl**, **amino**, **halo**, **carbonyl**,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkoxy**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$



branched or straight chain **alkenoxy**, **phenyloxy**, **benzyloxy**, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> **cycloalkyl**, **cyano**, **amido**, **thiol** **trifluoromethyl**, or **hydroxy** group; and

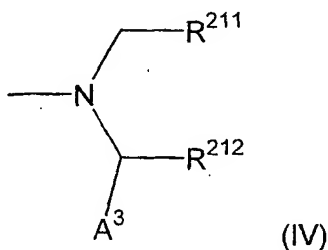
wherein A<sup>2</sup> is

- a **hydrogen** atom (-H); or a **carbaldehyde** (-CHO), a **ketone** group (-CO-R<sup>180</sup>), a **boronic acid** group (-B(OH)<sub>2</sub>), a **cyano** group (-C≡N), a **carboxylic acid** group (-COOH), a **carboxylic acid ester** group (-COOR<sup>181</sup>), a **carboxylic acid anhydride** group (-CO-O-CO-R<sup>182</sup>), a **hydroxamic acid** group (-CO-NH(OH)), a **N-substituted hydroxamic acid** group (-CO-NR<sup>183</sup>(OH)), a **O-substituted hydroxamic acid** group (-CO-NH(OR<sup>184</sup>)), a **carboxamide** group (-CO-NH<sub>2</sub>), a **N-substituted or N,N-disubstituted carboxylic acid amide** group, (-CO-NHR<sup>185</sup>; -CO-NR<sup>186</sup>R<sup>187</sup>), an **amido** group (-HN-CO-R<sup>188</sup>), a **sulfonic acid** group (-SO<sub>3</sub>H), a **sulfonamide** group (-SO<sub>2</sub>-NH<sub>2</sub>), a **N-substituted or N,N-disubstituted sulfonamide** group (-SO<sub>2</sub>-NHR<sup>189</sup>; -SO<sub>2</sub>-NR<sup>190</sup>R<sup>191</sup>), an **amidosulfone** group (-NH-SO<sub>2</sub>-R<sup>192</sup>), a **sulfone** group (-SO<sub>2</sub>-R<sup>193</sup>), a **phosphoric acid** group (-OP(=O)(OH)<sub>2</sub>), a **phosphoric acid ester** group (-OP(=O)(OR<sup>194</sup>)(OR<sup>195</sup>)), a **phosphonic acid** group (-P(=O)(OH)<sub>2</sub>), an **phosphonic acid ester** group (-P(=O)(OR<sup>196</sup>)(OR<sup>197</sup>)), a **halogen atom**, a **trifluormethyl** group (-CF<sub>3</sub>), a **thiol** group (-SH); a **thioether** group (-S-R<sup>198</sup>), a **hydroxy** group (-OH); an **alkoxy** group (-O-R<sup>199</sup>), a **tetrazole** group, an **amino** group (-NH<sub>2</sub>), or a **N-substituted or N,N-disubstituted amino** group (-NHR<sup>200</sup>; -NR<sup>201</sup>R<sup>202</sup>); and
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; and,
- wherein optionally, the pairs R<sup>186</sup>/R<sup>187</sup>, R<sup>190</sup>/R<sup>191</sup>, R<sup>194</sup>/R<sup>195</sup>, R<sup>196</sup>/R<sup>197</sup> and R<sup>201</sup>/R<sup>202</sup> independently of each other, may form a part of a **ring**; and
- wherein the substituents R<sup>180</sup>, R<sup>181</sup>, R<sup>182</sup>, R<sup>183</sup>, R<sup>184</sup>, R<sup>185</sup>, R<sup>186</sup>, R<sup>187</sup>, R<sup>188</sup>, R<sup>189</sup>, R<sup>190</sup>, R<sup>191</sup>, R<sup>192</sup>, R<sup>193</sup>, R<sup>194</sup>, R<sup>195</sup>, R<sup>196</sup>, R<sup>197</sup>, R<sup>198</sup>, R<sup>199</sup>, R<sup>200</sup>, R<sup>201</sup>, and R<sup>202</sup>, independently of each other are a **hydrogen** atom (-H), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**,

heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group;

or wherein the group PM

has the formula (IV)



- wherein  $R^{211}$  and  $R^{212}$ , independently of each other, are
- a **hydrogen** atom (-H); or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , and  $C_5$  branched or straight chain **alkyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkenyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkinyl**,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ , and  $C_7$  **cycloalkyl**, **aryl**, **heteroaryl** group or, an **amino** group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted **amino** group (-NHR<sup>240</sup>; -NR<sup>241</sup>R<sup>242</sup>); and
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; and,
- wherein optionally, **the pair**  $R^{211}/R^{212}$ , as well the pairs  $R^{226}/R^{227}$ ,  $R^{230}/R^{231}$ ,  $R^{234}/R^{235}$ ,  $R^{236}/R^{237}$  and  $R^{241}/R^{242}$ , independently of each other, may form a part of a ring; and
- wherein the substituents  $R^{220}$ ,  $R^{221}$ ,  $R^{222}$ ,  $R^{223}$ ,  $R^{224}$ ,  $R^{225}$ ,  $R^{226}$ ,  $R^{227}$ ,  $R^{228}$ ,  $R^{229}$ ,  $R^{230}$ ,  $R^{231}$ ,  $R^{232}$ ,  $R^{233}$ ,  $R^{234}$ ,  $R^{235}$ ,  $R^{236}$ ,  $R^{237}$ ,  $R^{238}$ ,  $R^{239}$ ,  $R^{240}$ ,  $R^{241}$ , and  $R^{242}$ , independently of each other, are a **hydrogen** atom (-H), or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , and  $C_5$  branched or straight chain **alkyl**, **aryl**, **heteroaryl**, **amino**, **halo**,

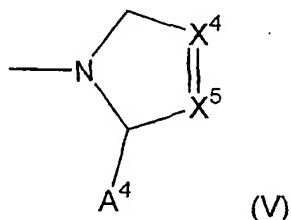
**carbonyl**, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, branched or straight chain **alkoxy**, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> branched or straight chain **alkenoxy**, **phenyloxy**, **benzyloxy**, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> **cycloalkyl**, **cyano**, **amido**, **thiol** **trifluoromethyl**, or **hydroxy** group; and

- wherein A<sup>3</sup> is
- a **hydrogen** atom (-H); or a **carbaldehyde** (-CHO), a **ketone** group (-CO-R<sup>260</sup>), a **boronic acid** group (-B(OH)<sub>2</sub>), a **cyano** group (-C≡N), a **carboxylic acid** group (-COOH), a **carboxylic acid ester** group (-COOR<sup>261</sup>), a **carboxylic acid anhydride** group (-CO-O-CO-R<sup>262</sup>), a **hydroxamic acid** group (-CO-NH(OH)), a **N-substituted hydroxamic acid** group (-CO-NR<sup>263</sup>(OH)), a **O-substituted hydroxamic acid** group (-CO-NH(OR<sup>264</sup>)), a **carboxamide** group (-CO-NH<sub>2</sub>), a **N-substituted or N,N-disubstituted carboxylic acid amide** group, (-CO-NHR<sup>265</sup>, -CO-NR<sup>266</sup>R<sup>267</sup>), an **amido** group (-HN-CO-R<sup>268</sup>), a **sulfonic acid** group (-SO<sub>3</sub>H), a **sulfonamide** group (-SO<sub>2</sub>-NH<sub>2</sub>), a **N-substituted or N,N-disubstituted sulfonamide** group (-SO<sub>2</sub>-NHR<sup>269</sup>, -SO<sub>2</sub>-NR<sup>270</sup>R<sup>271</sup>), an **amidosulfone** group (-NH-SO<sub>2</sub>-R<sup>272</sup>), a **sulfone** group (-SO<sub>2</sub>-R<sup>273</sup>), a **phosphoric acid** group (-OP(=O)(OH)<sub>2</sub>), a **phosphoric acid ester** group (-OP(=O)(OR<sup>274</sup>)(OR<sup>275</sup>)), a **phosphonic acid** group (-P(=O)(OH)<sub>2</sub>), an **phosphonic acid ester** group (-P(=O)(OR<sup>276</sup>)(OR<sup>277</sup>)), a **halogen atom**, a **trifluormethyl** group (-CF<sub>3</sub>), a **thiol** group (-SH); a **thioether** group (-S-R<sup>278</sup>), a **hydroxy** group (-OH); an **alkoxy** group (-O-R<sup>279</sup>), a **tetrazole** group, an **amino** group (-NH<sub>2</sub>), or a **N-substituted or N,N-disubstituted amino** group (-NHR<sup>280</sup>, -NR<sup>281</sup>R<sup>282</sup>); and
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; and,
- wherein optionally, the pairs R<sup>266</sup>/R<sup>267</sup>, R<sup>270</sup>/R<sup>271</sup>, R<sup>274</sup>/R<sup>275</sup>, R<sup>276</sup>/R<sup>277</sup> and R<sup>281</sup>/R<sup>282</sup>, independently of each other, may form a part of a **ring**; and
- wherein the substituents R<sup>260</sup>, R<sup>261</sup>, R<sup>262</sup>, R<sup>263</sup>, R<sup>264</sup>, R<sup>265</sup>, R<sup>266</sup>, R<sup>267</sup>, R<sup>268</sup>, R<sup>269</sup>, R<sup>270</sup>, R<sup>271</sup>, R<sup>272</sup>, R<sup>273</sup>, R<sup>274</sup>, R<sup>275</sup>, R<sup>276</sup>, R<sup>277</sup>, R<sup>278</sup>, R<sup>279</sup>, R<sup>280</sup>, R<sup>281</sup>, and R<sup>282</sup>, independently of each other are a **hydrogen** atom (-H), or an **alkyl**,

alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group;

or wherein the group PM

has the formula (V)



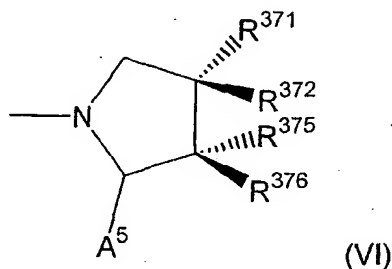
- wherein  $X^4$  is  $CR^{291}$  or N; and
- wherein  $X^5$  is  $CR^{292}$  or N; and
- wherein  $R^{291}$  and  $R^{292}$ , independently of each other, are
- a **hydrogen** atom (-H); or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , and  $C_5$  branched or straight chain **alkyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkenyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkynyl**,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ , and  $C_7$  **cycloalkyl**, **aryl**, **heteroaryl** group or an **amino** group ( $-NH_2$ ), or a N-substituted or N,N-disubstituted **amino** group ( $-NHR^{320}$ ,  $-NR^{321}R^{322}$ ); and
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the **the pair**  $R^{291}/R^{292}$ , if present, as well the pairs  $R^{306}/R^{307}$ ,  $R^{310}/R^{311}$ ,  $R^{314}/R^{315}$ ,  $R^{316}/R^{317}$  and  $R^{321}/R^{322}$ , independently of each other, may form a part of a **ring**; and

- wherein the substituents  $R^{300}$ ,  $R^{301}$ ,  $R^{302}$ ,  $R^{303}$ ,  $R^{304}$ ,  $R^{305}$ ,  $R^{306}$ ,  $R^{307}$ ,  $R^{308}$ ,  $R^{309}$ ,  $R^{310}$ ,  $R^{311}$ ,  $R^{312}$ ,  $R^{313}$ ,  $R^{314}$ ,  $R^{315}$ ,  $R^{316}$ ,  $R^{317}$ ,  $R^{318}$ ,  $R^{319}$ ,  $R^{320}$ ,  $R^{321}$ , and  $R^{322}$ , independently of each other are a **hydrogen atom (-H)**, or a **C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, and C<sub>5</sub> branched or straight chain alkyl, aryl, heteroaryl, amino, halo, carbonyl, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, branched or straight chain alkoxy, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> branched or straight chain alkenoxy, phenoxy, benzyloxy, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> cycloalkyl, cyano, amido, thiol trifluoromethyl, or hydroxy group**; and
- wherein A<sup>4</sup> is
- a **hydrogen atom (-H)**; or a **carbaldehyde (-CHO)**, a **ketone group (-CO-R<sup>340</sup>)**, a **boronic acid group (-B(OH)<sub>2</sub>)**, a **cyano group (-C≡N)**, a **carboxylic acid group (-COOH)**, a **carboxylic acid ester group (-COOR<sup>341</sup>)**, a **carboxylic acid anhydride group (-CO-O-CO-R<sup>342</sup>)**, a **hydroxamic acid group (-CO-NH(OH))**, a **N-substituted hydroxamic acid group (-CO-NR<sup>343</sup>(OH))**, a **O-substituted hydroxamic acid group (-CO-NH(OR<sup>344</sup>))**, a **carboxamide group (-CO-NH<sub>2</sub>)**, a **N-substituted or N,N-disubstituted carboxylic acid amide group, (-CO-NHR<sup>345</sup>, -CO-NR<sup>346</sup>R<sup>347</sup>)**, an **amido group (-HN-CO-R<sup>348</sup>)**, a **sulfonic acid group (-SO<sub>3</sub>H)**, a **sulfonamide group (-SO<sub>2</sub>-NH<sub>2</sub>)**, a **N-substituted or N,N-disubstituted sulfonamide group (-SO<sub>2</sub>-NHR<sup>349</sup>, -SO<sub>2</sub>-NR<sup>350</sup>R<sup>351</sup>)**, an **amidosulfone group (-NH-SO<sub>2</sub>-R<sup>352</sup>)**, a **sulfone group (-SO<sub>2</sub>-R<sup>353</sup>)**, a **phosphoric acid group (-OP(=O)(OH)<sub>2</sub>)**, a **phosphoric acid ester group (-OP(=O)(OR<sup>354</sup>)(OR<sup>355</sup>))**, a **phosphonic acid group (-P(=O)(OH)<sub>2</sub>)**, an **phosphonic acid ester group (-P(=O)(OR<sup>356</sup>)(OR<sup>357</sup>))**, a **halogen atom**, a **trifluoromethyl group (-CF<sub>3</sub>)**, a **thiol group (-SH)**; a **thioether group (-S-R<sup>358</sup>)**, a **hydroxy group (-OH)**; an **alkoxy group (-O-R<sup>359</sup>)**, a **tetrazole group**, an **amino group (-NH<sub>2</sub>)**, or a **N-substituted or N,N-disubstituted amino group (-NHR<sup>360</sup>, -NR<sup>361</sup>R<sup>362</sup>)**; and
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the pairs  $R^{346}/R^{347}$ ,  $R^{350}/R^{351}$ ,  $R^{354}/R^{355}$ ,  $R^{356}/R^{357}$  and  $R^{361}/R^{362}$ , independently of each other, may form a part of a **ring**; and

- wherein the substituents  $R^{340}$ ,  $R^{341}$ ,  $R^{342}$ ,  $R^{343}$ ,  $R^{344}$ ,  $R^{345}$ ,  $R^{346}$ ,  $R^{347}$ ,  $R^{348}$ ,  $R^{349}$ ,  $R^{350}$ ,  $R^{351}$ ,  $R^{352}$ ,  $R^{353}$ ,  $R^{354}$ ,  $R^{355}$ ,  $R^{356}$ ,  $R^{357}$ ,  $R^{358}$ ,  $R^{359}$ ,  $R^{360}$ ,  $R^{361}$ , and  $R^{362}$ , independently of each other are a **hydrogen** atom (-H), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

or wherein the group PM

has the formula (VI)



- wherein  $R^{371}$ ,  $R^{372}$ ,  $R^{375}$  and  $R^{376}$ , independently of each other, a **hydrogen** atom (-H); or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , and  $C_5$  branched or straight chain **alkyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkenyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkinyl**,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ , and  $C_7$  **cycloalkyl**, and **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group or, a **carbaldehyde** (-CHO), a **ketone** group (-CO- $R^{380}$ ), a **boronic acid** group (-B(OH)<sub>2</sub>), a **cyano** group (-C≡N), a **carboxylic acid** group (-COOH), a **carboxylic acid ester** group (-COOR<sup>381</sup>), a **halogen** atom, a **trifluormethyl** group (-CF<sub>3</sub>), a **thiol** group (-SH); a **thioether** group (-S- $R^{398}$ ), a **hydroxy** group (-OH); an **alkoxy** group (-O- $R^{399}$ ), a **tetrazole** group, an **amino** group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted **amino** group (-NHR<sup>400</sup>; -NR<sup>401</sup>R<sup>402</sup>); and

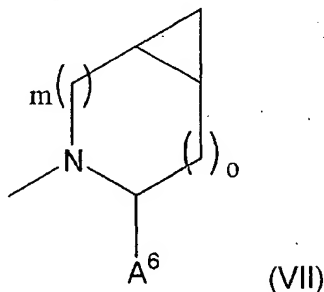
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, any **two of the groups**  $R^{371}$ ,  $R^{372}$ ,  $R^{375}$ , and  $R^{376}$ , as well as the pairs  $R^{386}/R^{387}$ ,  $R^{390}/R^{391}$ ,  $R^{394}/R^{395}$ ,  $R^{396}/R^{397}$  and  $R^{401}/R^{402}$ , independently of each other, may form a part of a **ring**; and
  - wherein the substituents  $R^{380}$ ,  $R^{381}$ ,  $R^{382}$ ,  $R^{383}$ ,  $R^{384}$ ,  $R^{385}$ ,  $R^{386}$ ,  $R^{387}$ ,  $R^{388}$ ,  $R^{389}$ ,  $R^{390}$ ,  $R^{391}$ ,  $R^{392}$ ,  $R^{393}$ ,  $R^{394}$ ,  $R^{395}$ ,  $R^{396}$ ,  $R^{397}$ ,  $R^{398}$ ,  $R^{399}$ ,  $R^{400}$ ,  $R^{401}$ , and  $R^{402}$ , independently of each other are a **hydrogen atom (-H)**, or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , and  $C_5$  branched or straight chain **alkyl**, **aryl**, **heteroaryl**, **amino**, **halo**, **carbonyl**,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkoxy**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  branched or straight chain **alkenoxy**, **phenyloxy**, **benzyloxy**,  $C_3$ ,  $C_4$ ,  $C_5$  **cycloalkyl**, **cyano**, **amido**, **thiol trifluoromethyl**, or **hydroxy group**; and
- **alternatively**; the two groups  $R^{371}$  and  $R^{372}$  can be together an **oxo (=O)** or **hydroxyimino (=N-OH)** group; and
- **alternatively**; the two groups  $R^{375}$  and  $R^{376}$  can be together an **oxo (=O)** or **hydroxyimino (=N-OH)** group; and
- **wherein  $A^5$  is**
  - a **hydrogen atom (-H)**; or a **carbaldehyde (-CHO)**, a **ketone group (-CO- $R^{420}$ )**, a **boronic acid group (-B(OH)<sub>2</sub>)**, a **cyano group (-C≡N)**, a **carboxylic acid group (-COOH)**, a **carboxylic acid ester group (-COOR<sup>421</sup>)**, a **carboxylic acid anhydride group (-CO-O-CO- $R^{422}$ )**, a **hydroxamic acid group (-CO-NH(OH))**, a **N-substituted hydroxamic acid group (-CO-NR<sup>423</sup>(OH))**, a **O-substituted hydroxamic acid group (-CO-NH(OR<sup>424</sup>))**, a **carboxamide group (-CO-NH<sub>2</sub>)**, a **N-substituted or N,N-disubstituted carboxylic acid amide group, (-CO-NHR<sup>425</sup>; -CO-NR<sup>426</sup>R<sup>427</sup>)**, an **amido group (-HN-CO- $R^{428}$ )**, a **sulfonic acid group (-SO<sub>3</sub>H)**, a **sulfonamide group (-SO<sub>2</sub>-NH<sub>2</sub>)**, a **N-substituted or N,N-disubstituted sulfonamide group (-SO<sub>2</sub>-NHR<sup>429</sup>; -SO<sub>2</sub>-NR<sup>430</sup>R<sup>431</sup>)**, an **amidosulfone group**

(-NH-SO<sub>2</sub>-R<sup>432</sup>), a **sulfone** group (-SO<sub>2</sub>-R<sup>433</sup>), a **phosphoric acid** group (-OP(=O)(OH)<sub>2</sub>), a **phosphoric acid ester** group (-OP(=O)(OR<sup>434</sup>)(OR<sup>435</sup>)), a **phosphonic acid** group (-P(=O)(OH)<sub>2</sub>), an **phosphonic acid ester** group (-P(=O)(OR<sup>436</sup>)(OR<sup>437</sup>)), a **halogen atom**, a **trifluormethyl** group (-CF<sub>3</sub>), a **thiol** group (-SH); a **thioether** group (-S-R<sup>438</sup>), a **hydroxy** group (-OH); an **alkoxy** group (-O-R<sup>439</sup>), a **tetrazole** group, an **amino** group (-NH<sub>2</sub>), or a **N-substituted** or **N,N-disubstituted amino** group (-NHR<sup>440</sup>; -NR<sup>441</sup>R<sup>442</sup>); and

- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the pairs R<sup>426</sup>/R<sup>427</sup>, R<sup>430</sup>/R<sup>431</sup>, R<sup>434</sup>/R<sup>435</sup>, R<sup>436</sup>/R<sup>437</sup> and R<sup>441</sup>/R<sup>442</sup>, independently of each other, may form a part of a **ring**; and
- wherein the substituents R<sup>420</sup>, R<sup>421</sup>, R<sup>422</sup>, R<sup>423</sup>, R<sup>424</sup>, R<sup>425</sup>, R<sup>426</sup>, R<sup>427</sup>, R<sup>428</sup>, R<sup>429</sup>, R<sup>430</sup>, R<sup>431</sup>, R<sup>432</sup>, R<sup>433</sup>, R<sup>434</sup>, R<sup>435</sup>, R<sup>436</sup>, R<sup>437</sup>, R<sup>438</sup>, R<sup>439</sup>, R<sup>440</sup>, R<sup>441</sup>, and R<sup>442</sup>, independently of each other are a **hydrogen** atom (-H), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

or wherein the group **PM**

has the formula (VII)



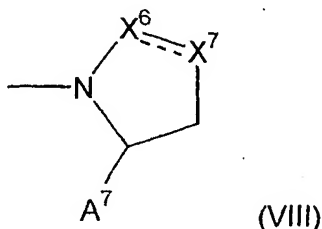


- wherein m is equal to 1 or 2, and o is equal to 1 or 2, and m or o can be equal to 0;
- wherein  $A^6$  is a **hydrogen atom** (-H); or a **carbaldehyde** (-CHO), a **ketone group** (-CO-R<sup>460</sup>), a **boronic acid** group (-B(OH)<sub>2</sub>), a **cyano** group (-C≡N), a **carboxylic acid** group (-COOH), a **carboxylic acid ester** group (-COOR<sup>461</sup>), a **carboxylic acid anhydride** group (-CO-O-CO-R<sup>462</sup>), a **hydroxamic acid** group (-CO-NH(OH)), a **N-substituted hydroxamic acid** group (-CO-NR<sup>463</sup>(OH)), a **O-substituted hydroxamic acid** group (-CO-NH(OR<sup>464</sup>)), a **carboxamide** group (-CO-NH<sub>2</sub>), a **N-substituted or N,N-disubstituted carboxylic acid amide** group, (-CO-NHR<sup>465</sup>; -CO-NR<sup>466</sup>R<sup>467</sup>), an **amido** group (-HN-CO-R<sup>468</sup>), a **sulfonic acid** group (-SO<sub>3</sub>H), a **sulfonamide** group (-SO<sub>2</sub>-NH<sub>2</sub>), a **N-substituted or N,N-disubstituted sulfonamide** group (-SO<sub>2</sub>-NHR<sup>469</sup>; -SO<sub>2</sub>-NR<sup>470</sup>R<sup>471</sup>), an **amidosulfone** group (-NH-SO<sub>2</sub>-R<sup>472</sup>), a **sulfone** group (-SO<sub>2</sub>-R<sup>473</sup>), a **phosphoric acid** group (-OP(=O)(OH)<sub>2</sub>), a **phosphoric acid ester** group (-OP(=O)(OR<sup>474</sup>)(OR<sup>475</sup>)), a **phosphonic acid** group (-P(=O)(OH)<sub>2</sub>), an **phosphonic acid ester** group (-P(=O)(OR<sup>476</sup>)(OR<sup>477</sup>)), a **halogen atom**, a **trifluormethyl** group (-CF<sub>3</sub>), a **thiol** group (-SH); a **thioether** group (-S-R<sup>478</sup>), a **hydroxy** group (-OH); an **alkoxy** group (-O-R<sup>479</sup>), a **tetrazole** group, an **amino** group (-NH<sub>2</sub>), or a **N-substituted or N,N-disubstituted amino** group (-NHR<sup>480</sup>; -NR<sup>481</sup>R<sup>482</sup>);
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the pairs R<sup>466</sup>/R<sup>467</sup>, R<sup>470</sup>/R<sup>471</sup>, R<sup>474</sup>/R<sup>475</sup>, R<sup>476</sup>/R<sup>477</sup> and R<sup>481</sup>/R<sup>482</sup>, independently of each other, may form a part of a **ring**; **and**
- wherein the substituents R<sup>460</sup>, R<sup>461</sup>, R<sup>462</sup>, R<sup>463</sup>, R<sup>464</sup>, R<sup>465</sup>, R<sup>466</sup>, R<sup>467</sup>, R<sup>468</sup>, R<sup>469</sup>, R<sup>470</sup>, R<sup>471</sup>, R<sup>472</sup>, R<sup>473</sup>, R<sup>474</sup>, R<sup>475</sup>, R<sup>476</sup>, R<sup>477</sup>, R<sup>478</sup>, R<sup>479</sup>, R<sup>480</sup>, R<sup>481</sup>, and R<sup>482</sup>, independently of each other are a **hydrogen atom** (-H), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**,

heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group;

or wherein the group PM

has the formula (VIII)



- wherein  $X^6$  is selected from  $CR^{490}R^{491}$ , O, S or  $NR^{492}$ , when the bond between  $X^6$  and  $X^7$  is a single bond; and
- wherein  $X^7$  is selected from  $CR^{493}R^{494}$ , O, S, or  $NR^{495}$ , when the bond between  $X^6$  and  $X^7$  is a single bond;
- **or alternatively,**
- wherein  $X^6$  is selected from  $CR^{496}$  or N, when the bond between  $X^6$  and  $X^7$  is a double bond; and
- wherein  $X^7$  is selected from  $CR^{497}$  or N, when the bond between  $X^6$  and  $X^7$  is a double bond; and
- wherein  $R^{490}$ ,  $R^{491}$ ,  $R^{492}$ ,  $R^{493}$ ,  $R^{494}$ ,  $R^{495}$ ,  $R^{496}$ , and  $R^{497}$ , independently of each other, are a **hydrogen** atom (-H); or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , and  $C_5$  branched or straight chain **alkyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkenyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkinyl**,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ , and  $C_7$  **cycloalkyl**, **aryl**, **heteroaryl** group, or an **amino** group ( $-NH_2$ ), or a N-substituted or N,N-disubstituted **amino** group ( $-NHR^{520}$ ;  $-NR^{521}R^{522}$ ); and

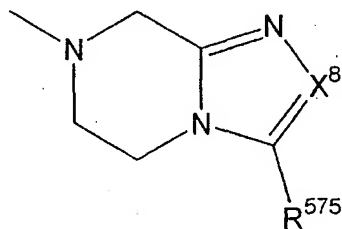
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, any two the groups  $R^{490}$ ,  $R^{491}$ ,  $R^{492}$ ,  $R^{493}$ ,  $R^{494}$ ,  $R^{495}$ ,  $R^{496}$ , and  $R^{497}$ , if present, as well as the pairs  $R^{506}/R^{507}$ ,  $R^{510}/R^{511}$ ,  $R^{514}/R^{515}$ ,  $R^{516}/R^{517}$  and  $R^{521}/R^{522}$ , independently of each other, may form a part of a **ring**; and
- wherein the substituents  $R^{500}$ ,  $R^{501}$ ,  $R^{502}$ ,  $R^{503}$ ,  $R^{504}$ ,  $R^{505}$ ,  $R^{506}$ ,  $R^{507}$ ,  $R^{508}$ ,  $R^{509}$ ,  $R^{510}$ ,  $R^{511}$ ,  $R^{512}$ ,  $R^{513}$ ,  $R^{514}$ ,  $R^{515}$ ,  $R^{516}$ ,  $R^{517}$ ,  $R^{518}$ ,  $R^{519}$ ,  $R^{520}$ ,  $R^{521}$ , and  $R^{522}$ , independently of each other are a **hydrogen atom** (-H), or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , and  $C_5$  branched or straight chain **alkyl**, **aryl**, **heteroaryl**, **amino**, **halo**, **carbonyl**,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkoxy**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  branched or straight chain **alkenoxy**, **phenyloxy**, **benzyloxy**,  $C_3$ ,  $C_4$ ,  $C_5$  **cycloalkyl**, **cyano**, **amido**, **thiol** **trifluoromethyl**, or **hydroxy** group; and
- wherein  $A^7$  is
- a **hydrogen atom** (-H); or a **carbaldehyde** (-CHO), a **ketone** group (-CO- $R^{540}$ ), a **boronic acid** group (-B(OH)<sub>2</sub>), a **cyano** group (-C≡N), a **carboxylic acid** group (-COOH), a **carboxylic acid ester** group (-COOR<sup>541</sup>), a **carboxylic acid anhydride** group (-CO-O-CO- $R^{542}$ ), a **hydroxamic acid** group (-CO-NH(OH)), a **N-substituted hydroxamic acid** group (-CO-NR<sup>543</sup>(OH)), a **O-substituted hydroxamic acid** group (-CO-NH(OR<sup>544</sup>)), a **carboxamide** group (-CO-NH<sub>2</sub>), a **N-substituted or N,N-disubstituted carboxylic acid amide** group, (-CO-NHR<sup>545</sup>; -CO-NR<sup>546</sup>R<sup>547</sup>), an **amido** group (-HN-CO- $R^{548}$ ), a **sulfonic acid** group (-SO<sub>3</sub>H), a **sulfonamide** group (-SO<sub>2</sub>-NH<sub>2</sub>), a **N-substituted or N,N-disubstituted sulfonamide** group (-SO<sub>2</sub>-NHR<sup>549</sup>; -SO<sub>2</sub>-NR<sup>550</sup>R<sup>551</sup>), an **amidosulfone** group (-NH-SO<sub>2</sub>-R<sup>552</sup>), a **sulfone** group (-SO<sub>2</sub>-R<sup>553</sup>), a **phosphoric acid** group (-OP(=O)(OH)<sub>2</sub>), a **phosphoric acid ester** group (-OP(=O)(OR<sup>554</sup>)(OR<sup>555</sup>)), a **phosphonic acid** group (-P(=O)(OH)<sub>2</sub>), an **phosphonic acid ester** group (-P(=O)(OR<sup>556</sup>)(OR<sup>557</sup>)), a **halogen atom**, a **trifluormethyl** group (-CF<sub>3</sub>), a **thiol** group (-SH); a **thioether** group (-S-R<sup>558</sup>), a **hydroxy** group (-OH); an **alkoxy**

group ( $-O-R^{559}$ ), a **tetrazole** group, an **amino** group ( $-NH_2$ ), or a N-substituted or N,N-disubstituted **amino** group ( $-NHR^{560}$ ;  $-NR^{561}R^{562}$ ); and

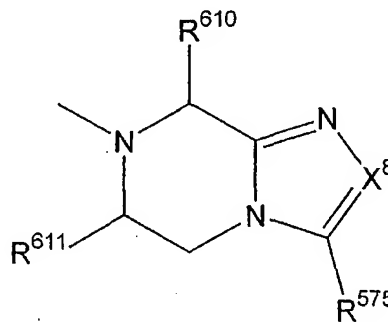
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; and,
- wherein optionally, the pairs  $R^{546}/R^{547}$ ,  $R^{550}/R^{551}$ ,  $R^{554}/R^{555}$ ,  $R^{556}/R^{557}$  and  $R^{561}/R^{562}$ , independently of each other, may form a part of a **ring**; and
- wherein the substituents  $R^{540}$ ,  $R^{541}$ ,  $R^{542}$ ,  $R^{543}$ ,  $R^{544}$ ,  $R^{545}$ ,  $R^{546}$ ,  $R^{547}$ ,  $R^{548}$ ,  $R^{549}$ ,  $R^{550}$ ,  $R^{551}$ ,  $R^{552}$ ,  $R^{553}$ ,  $R^{554}$ ,  $R^{555}$ ,  $R^{556}$ ,  $R^{557}$ ,  $R^{558}$ ,  $R^{559}$ ,  $R^{560}$ ,  $R^{561}$ , and  $R^{562}$ , independently of each other are a **hydrogen** atom ( $-H$ ), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

or wherein the group **PM**

has the formula (IX) or (IXa)



(IX)



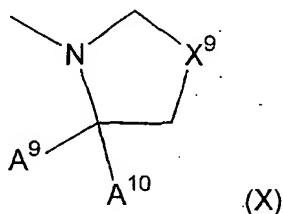
(IXa)

- wherein  $X^8$  is N or  $CR^{570}$ ; and
- wherein  $R^{570}$ ,  $R^{575}$ ,  $R^{610}$  and  $R^{611}$  independently of each other, are  
a **hydrogen** atom (-H); or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , and  $C_5$  branched or straight chain **alkyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkenyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkinyl**,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ , and  $C_7$  **cycloalkyl**, **aryl**, **heteroaryl** group, or a **carbaldehyde** (-CHO), a **ketone** group (-CO- $R^{580}$ ), a **boronic acid** group (-B(OH)<sub>2</sub>), a **cyano** group (-C≡N), a **carboxylic acid** group (-COOH), a **carboxylic acid ester** group (-COOR<sup>581</sup>), a **carboxylic acid anhydride** group (-CO-O-CO- $R^{582}$ ), a **hydroxamic acid** group (-CO-NH(OH)), a N-substituted **hydroxamic acid** group (-CO-NR<sup>583</sup>(OH)), a O-substituted **hydroxamic acid** group (-CO-NH(OR<sup>584</sup>)), a **carboxamide** group (-CO-NH<sub>2</sub>), a N-substituted or N,N-disubstituted **carboxylic acid amide** group, (-CO-NHR<sup>585</sup>; -CO-NR<sup>586</sup>R<sup>587</sup>), an **amido** group (-HN-CO- $R^{588}$ ), a **sulfonic acid** group (-SO<sub>3</sub>H), a **sulfonamide** group (-SO<sub>2</sub>-NH<sub>2</sub>), a N-substituted or N,N-disubstituted **sulfonamide** group (-SO<sub>2</sub>-NHR<sup>589</sup>; -SO<sub>2</sub>-NR<sup>590</sup>R<sup>591</sup>), an **amidosulfone** group (-NH-SO<sub>2</sub>- $R^{592}$ ), a **sulfone** group (-SO<sub>2</sub>- $R^{593}$ ), a **phosphoric acid** group (-OP(=O)(OH)<sub>2</sub>), a **phosphoric acid ester** group (-OP(=O)(OR<sup>594</sup>)(OR<sup>595</sup>)), a **phosphonic acid** group (-P(=O)(OH)<sub>2</sub>), an **phosphonic acid ester** group (-P(=O)(OR<sup>596</sup>)(OR<sup>597</sup>)), a **halogen** atom, a **trifluormethyl** group (-CF<sub>3</sub>), a **thiol** group (-SH); a **thioether** group (-S- $R^{598}$ ), a **hydroxy** group (-OH); an **alkoxy** group (-O- $R^{599}$ ), a **tetrazole** group, an **amino** group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted **amino** group (-NHR<sup>600</sup>; -NR<sup>601</sup>R<sup>602</sup>);
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; and,
- wherein optionally, the pairs  $R^{570}/R^{575}$ , if present, as well as the pairs  $R^{586}/R^{587}$ ,  $R^{590}/R^{591}$ ,  $R^{594}/R^{595}$ ,  $R^{596}/R^{597}$  and  $R^{601}/R^{602}$ , independently of each other, may form a part of a **ring**; and
- wherein the substituents  $R^{580}$ ,  $R^{581}$ ,  $R^{582}$ ,  $R^{583}$ ,  $R^{584}$ ,  $R^{585}$ ,  $R^{586}$ ,  $R^{587}$ ,  $R^{588}$ ,  $R^{589}$ ,  $R^{590}$ ,  $R^{591}$ ,  $R^{592}$ ,  $R^{593}$ ,  $R^{594}$ ,  $R^{595}$ ,  $R^{596}$ ,  $R^{597}$ ,  $R^{598}$ ,  $R^{599}$ ,  $R^{600}$ ,  $R^{601}$ , and

$R^{602}$ , independently of each other are a **hydrogen** atom (-H), or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , and  $C_5$  branched or straight chain **alkyl**, **aryl**, **heteroaryl**, **amino**, **halo**, **carbonyl**,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkoxy**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  branched or straight chain **alkenoxy**, **phenyloxy**, **benzyloxy**,  $C_3$ ,  $C_4$ ,  $C_5$  **cycloalkyl**, **cyano**, **amido**, **thiol** **trifluoromethyl**, or **hydroxy** group; and

or wherein the group **PM**

has the formula (X)



- wherein the groups  $X^9$  is  $CR^{900}R^{901}$ , S, SO, SO<sub>2</sub> or  $NR^{902}$ 
  - wherein  $R^{900}$ ,  $R^{901}$  and  $R^{902}$ , are, independently of each other, selected from hydrogen, fluorine,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens, or  $-C(=O)NR^{910}R^{911}$ .
- wherein  $A^9$  and  $A^{10}$  are, independently of each other, selected from hydrogen, cyano,  $-C(=O)NR^{912}R^{913}$ , or  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein

- $R^{910}$  and  $R^{912}$ , are, independently of each other, selected from hydrogen, or  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens; and

- $R^{911}$  and  $R^{913}$ , are, independently of each other, selected from the group consisting of

(1) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5, substituents independently selected from halogen and  $R^{920}$ ;

(2)  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6 or 7 substituents independently selected from (a) 0, 1, 2, 3, 4, or 5 halogens, and (b) 0, 1, 2 substituents selected from the group consisting of

- (a) hydroxy,
- (b)  $-COOH$ ,
- (c)  $-COO(C_1, C_2, C_3, C_4, C_5 \text{ or } C_6 \text{ alkyl})$ , i.e. ester,
- (d) phenyl,
- (e) naphthyl,
- (f)  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  cycloalkyl,
- (g) a 5 - or 6 membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur;
- (h) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (a) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (b) a benzene ring fused to a 5- or 6-membered heterocycle having 1, 2, or 3 hetero atoms;

- wherein said  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  cycloalkyl, phenyl, naphthyl, are optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from halogen and  $R^{920}$ , and said 5 or 6 membered heterocycle and said 8, 9 or 10 - membered bicyclic ring system are each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, and  $R^{920}$ ; and

(3) C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, which is optionally substituted with 1, 2, or 3 groups independently selected from halogen, hydroxy, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein R<sup>920</sup> is selected from the group consisting of:

- (1) hydroxy;
- (2) cyano;
- (3) C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl optionally substituted with 1, 2, or 3 groups independently selected from halogen, hydroxy, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, wherein said -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl are linear or branched and are optionally substituted with 1, 2, 3, 4, 5 or 6 substituents selected from 1, 2, 3, 4, or 5 halogens, and 0 or 1 substituents selected from -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, -COOH, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl substituents being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;
- (4) C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub>, C<sub>9</sub> or C<sub>10</sub> alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6, or 7 substituents independently selected from 0, 1, 2, 3, 4, or 5 halogen atoms and 0, 1, or 2 groups selected from

- (a) hydroxy;
- (b) -COOH;
- (c) -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, which may linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens;
- (d) a 5 - or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, optionally substituted with 1, 2, or 3



substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(e) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (i) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (ii) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(f) -CONR<sup>925</sup>R<sup>925</sup>;

(g) -SO<sub>2</sub>NR<sup>925</sup>R<sup>925</sup>;

(h) -NR<sup>925</sup>-C(=O)R<sup>925</sup>

(i) -NR<sup>925</sup>-C(=O)NR<sup>925</sup>R<sup>925</sup>;

(j) -NR<sup>925</sup>COOR<sup>930</sup>

(k) -O-CO-R<sup>930</sup>

(l) -O-CO-NR<sup>925</sup>R<sup>925</sup>;

(m) -NR<sup>925</sup>SO<sub>2</sub>R<sup>930</sup>;

(n) -NR<sup>925</sup>R<sup>925</sup>;

(o) phenyl which is optionally substituted with 1, 2, 3, 4, or 5 group independently selected from halogen, hydroxy, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester being linear or branched and optionally substituted

with 1, 2, 3, 4, 5, or 6 substituents independently selected from 0 or 1

C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl and 0, 1, 2, 3, 4, or 5 halogens, and

(p) C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl, which is optionally substituted with 1, 2, 3, 4, 5, or 6 halogens;

(5) OC<sub>1</sub>, OC<sub>2</sub>, OC<sub>3</sub>, OC<sub>4</sub>, OC<sub>5</sub>, OC<sub>6</sub>, OC<sub>7</sub>, OC<sub>8</sub>, OC<sub>9</sub> or OC<sub>10</sub> alkyl, which is linear or branched and is optionally substituted with 0, 1, 2, 3, 4, or 5 halogen atoms and 0, 1, or 2 substituents selected from

(a) hydroxy;

(b) -COOH;

(c) -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, which may be linear or branched and is optionally substituted with 1, 2, 3, 4 or 5 halogens;

(d) a 5- or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.;

(e) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (i) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (ii) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(f) -CONR<sup>925</sup>R<sup>925</sup>;

(g)  $-\text{SO}_2\text{NR}^{925}\text{R}^{925}$ ;

(h)  $-\text{NR}^{925}-\text{C}(=\text{O})\text{R}^{925}$

(i)  $-\text{NR}^{925}-\text{C}(=\text{O})\text{NR}^{925}\text{R}^{925}$ ;

(j)  $-\text{NR}^{925}\text{COOR}^{930}$

(k)  $-\text{O}-\text{CO}-\text{R}^{930}$

(l)  $-\text{O}-\text{CO}-\text{NR}^{925}\text{R}^{925}$ ;

(m)  $-\text{NR}^{925}\text{SO}_2\text{R}^{930}$ ;

(n)  $-\text{NR}^{925}\text{R}^{925}$ ;

(o) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5 groups independently selected from halogen, hydroxy,  $\text{C}_1$ ,  $\text{C}_2$ ,  $\text{C}_3$ ,  $\text{C}_4$ ,  $\text{C}_5$  or  $\text{C}_6$  alkyl,  $-\text{OC}_1$ ,  $-\text{OC}_2$ ,  $-\text{OC}_3$ ,  $-\text{OC}_4$ ,  $-\text{OC}_5$  or  $-\text{OC}_6$  alkyl,  $-\text{COOH}$ ,  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester, said  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  alkyl,  $-\text{OC}_1$ ,  $-\text{OC}_2$ ,  $-\text{OC}_3$ ,  $-\text{OC}_4$ ,  $-\text{OC}_5$  or  $-\text{OC}_6$  alkyl,  $-\text{COOH}$ ,  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, 5, or 6 substituents independently selected from 0 or 1  $\text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  cycloalkyl and 0, 1, 2, 3, 4, or 5 halogens, and

(p)  $\text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  cycloalkyl, which is optionally substituted with 1, 2, 3, 4, 5, or 6 halogens;

(6)  $-\text{COOH}$ ;

(7)  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester, which may be linear or branched and is optionally substituted with 1, 2, 3, 4, 5 halogens;

(8) a 5 - or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, said heterocycle being optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen,  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5$  or  $-\text{OC}_6$  alkyl, said  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5$  or  $-\text{OC}_6$  alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.

(9) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (a) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen,

oxygen or sulfur, or (b) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(10) -CONR<sup>925</sup>R<sup>925</sup>;

(11) -SO<sub>2</sub>NR<sup>925</sup>R<sup>925</sup>;

(12) -NR<sup>925</sup>-C(=O)R<sup>925</sup>

(13) -NR<sup>925</sup>-C(=O)NR<sup>925</sup>R<sup>925</sup>;

(14) -NR<sup>925</sup>COOR<sup>930</sup>

(15) -O-CO-R<sup>930</sup>

(16) -O-CO-NR<sup>925</sup>R<sup>925</sup>;

(17) -NR<sup>925</sup>SO<sub>2</sub>R<sup>930</sup>;

(18) -NR<sup>925</sup>R<sup>925</sup>;

(19) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5 group independently selected from halogen, hydroxy, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

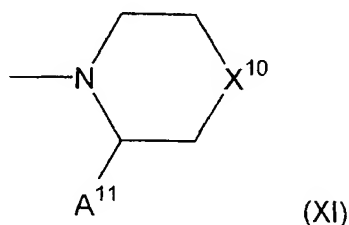
wherein R<sup>930</sup> is selected from the group consisting of phenyl, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl, and C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl, wherein C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6, substituents independently selected from 0, 1, 2, 3, 4, or 5 halogens, 0 or 1 phenyl, wherein said optional phenyl substituent and said R<sup>930</sup>, when R<sup>930</sup> is phenyl or C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl, are optionally substituted with 1, 2, 3, 4, or 5 substituents, independently selected from

halogen, OH, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, or C<sub>5</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, or -OC<sub>5</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, or C<sub>5</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, or -OC<sub>5</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.

wherein R<sup>925</sup> is selected from R<sup>930</sup> and hydrogen.

wherein the group PM

has the formula (XI)



- wherein the groups X<sup>10</sup> is CR<sup>1000</sup>R<sup>1001</sup>, S, SO, SO<sub>2</sub> or NR<sup>1002</sup>
  - wherein R<sup>1000</sup>, R<sup>1001</sup> and R<sup>1002</sup>, are, independently of each other, selected from hydrogen, fluorine, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens, or -C(=O)NR<sup>1010</sup>R<sup>1011</sup>.

and A<sup>11</sup> is selected from

hydrogen, cyano, -C(=O)NR<sup>1012</sup>R<sup>1013</sup>, or C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein

- R<sup>1010</sup> and R<sup>1012</sup>, are, independently of each other, selected from hydrogen, or C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens; and

- $R^{1011}$  and  $R^{1013}$ , are, independently of each other, selected from the group consisting of

(1) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5, substituents independently selected from halogen and  $R^{1020}$ ;

(2)  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6 or 7 substituents independently selected from (a) 0, 1, 2, 3, 4, or 5 halogens, and (b) 0, 1, 2 substituents selected from the group consisting of

- (a) hydroxy,
- (b)  $-COOH$ ,
- (c)  $-COO(C_1, C_2, C_3, C_4, C_5 \text{ or } C_6 \text{ alkyl})$ , i.e. ester,
- (d) phenyl,
- (e) naphthyl,
- (f)  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  cycloalkyl,
- (g) a 5 - or 6 membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur;
- (h) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (a) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (b) a benzene ring fused to a 5- or 6-membered heterocycle having 1, 2, or 3 hetero atoms;

- wherein said  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  cycloalkyl, phenyl, naphthyl, are optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from halogen and  $R^{1020}$ , and said 5 or 6 membered heterocycle and said 8, 9 or 10 - membered bicyclic ring system are each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, and  $R^{1020}$ ; and

(3) C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, which is optionally substituted with 1, 2, or 3 groups independently selected from halogen, hydroxy, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein R<sup>1020</sup> is selected from the group consisting of:

- (1) hydroxy;
- (2) cyano;
- (3) C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl optionally substituted with 1, 2, or 3 groups independently selected from halogen, hydroxy, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, wherein said -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl are linear or branched and are optionally substituted with 1, 2, 3, 4, 5 or 6 substituents selected from 1, 2, 3, 4, or 5 halogens, and 0 or 1 substituents selected from -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, -COOH, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl substituents being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;
- (4) C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub>, C<sub>9</sub> or C<sub>10</sub> alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6, or 7 substituents independently selected from 0, 1, 2, 3, 4, or 5 halogen atoms and 0, 1, or 2 groups selected from
  - (a) hydroxy;
  - (b) -COOH;
  - (c) -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, which may linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens;
  - (d) a 5 - or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, optionally substituted with 1, 2, or 3

substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.;

(e) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (i) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (ii) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(f) -CONR<sup>1025</sup>R<sup>1025</sup>;

(g) -SO<sub>2</sub>NR<sup>1025</sup>R<sup>1025</sup>;

(h) -NR<sup>1025</sup>-C(=O)R<sup>1025</sup>;

(i) -NR<sup>1025</sup>-C(=O)NR<sup>1025</sup>R<sup>1025</sup>;

(j) -NR<sup>1025</sup>COOR<sup>1030</sup>

(k) -O-CO-R<sup>1030</sup>

(l) -O-CO-NR<sup>1025</sup>R<sup>1025</sup>;

(m) -NR<sup>1025</sup>SO<sub>2</sub>R<sup>1030</sup>;

(n) -NR<sup>1025</sup>R<sup>1025</sup>;

(o) phenyl which is optionally substituted with 1, 2, 3, 4, or 5 group independently selected from halogen, hydroxy, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester being linear or branched and optionally substituted



with 1, 2, 3, 4, 5, or 6 substituents independently selected from 0 or 1

C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl and 0, 1, 2, 3, 4, or 5 halogens, and

(p) C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, which is optionally substituted with 1, 2, 3, 4, 5, or 6 halogens;

(5) OC<sub>1</sub>, OC<sub>2</sub>, OC<sub>3</sub>, OC<sub>4</sub>, OC<sub>5</sub>, OC<sub>6</sub>, OC<sub>7</sub>, OC<sub>8</sub>, OC<sub>9</sub> or OC<sub>10</sub> alkyl, which is linear or branched and is optionally substituted with 0, 1, 2, 3, 4, or 5 halogen atoms and 0, 1, or 2 substituents selected from

(a) hydroxy;

(b)-COOH;

(c) -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, which may be linear or branched and is optionally substituted with 1, 2, 3, 4 or 5 halogens;

(d) a 5 - or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.;

(e) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (i) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (ii) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(f) -CONR<sup>1025</sup>R<sup>1025</sup>;

- (g)  $-\text{SO}_2\text{NR}^{1025}\text{R}^{1025}$ ;
- (h)  $-\text{NR}^{1025}-\text{C}(=\text{O})\text{R}^{1025}$
- (i)  $-\text{NR}^{1025}-\text{C}(=\text{O})\text{NR}^{1025}\text{R}^{1025}$ ;
- (j)  $-\text{NR}^{1025}\text{COOR}^{1030}$
- (k)  $-\text{O}-\text{CO}-\text{R}^{1030}$
- (l)  $-\text{O}-\text{CO}-\text{NR}^{1025}\text{R}^{1025}$ ;
- (m)  $-\text{NR}^{1025}\text{SO}_2\text{R}^{1030}$ ;
- (n)  $-\text{NR}^{1025}\text{R}^{1025}$ ;
- (o) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5 groups independently selected from halogen, hydroxy,  $\text{C}_1$ ,  $\text{C}_2$ ,  $\text{C}_3$ ,  $\text{C}_4$ ,  $\text{C}_5$  or  $\text{C}_6$  alkyl,  $-\text{OC}_1$ ,  $-\text{OC}_2$ ,  $-\text{OC}_3$ ,  $-\text{OC}_4$ ,  $-\text{OC}_5$  or  $-\text{OC}_6$  alkyl,  $-\text{COOH}$ ,  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester, said  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  alkyl,  $-\text{OC}_1$ ,  $-\text{OC}_2$ ,  $-\text{OC}_3$ ,  $-\text{OC}_4$ ,  $-\text{OC}_5$  or  $-\text{OC}_6$  alkyl,  $-\text{COOH}$ ,  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, 5, or 6 substituents independently selected from 0 or 1  $\text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  cycloalkyl and 0, 1, 2, 3, 4, or 5 halogens, and
- (p)  $\text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  cycloalkyl, which is optionally substituted with 1, 2, 3, 4, 5, or 6 halogens;
- (6)  $-\text{COOH}$ ;
- (7)  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester, which may be linear or branched and is optionally substituted with 1, 2, 3, 4, 5 halogens;
- (8) a 5- or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, said heterocycle being optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen,  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5$  or  $-\text{OC}_6$  alkyl, said  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5$  or  $-\text{OC}_6$  alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.
- (9) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (a) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen,

oxygen or sulfur, or (b) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(10) -CONR<sup>1025</sup>R<sup>1025</sup>;

(11) -SO<sub>2</sub>NR<sup>1025</sup>R<sup>1025</sup>;

(12) -NR<sup>1025</sup>-C(=O)R<sup>1025</sup>

(13) -NR<sup>1025</sup>-C(=O)NR<sup>1025</sup>R<sup>1025</sup>;

(14) -NR<sup>925</sup>COOR<sup>1030</sup>

(15) -O-CO-R<sup>1030</sup>

(16) -O-CO-NR<sup>1025</sup>R<sup>1025</sup>;

(17) -NR<sup>1025</sup>SO<sub>2</sub>R<sup>1030</sup>;

(18) - NR<sup>1025</sup>R<sup>1025</sup>;

(19) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5 group independently selected from halogen, hydroxy, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

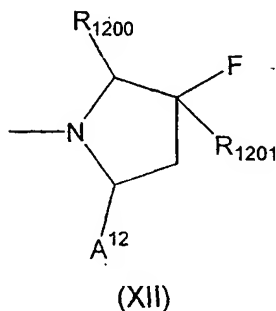
wherein R<sup>1030</sup> is selected from the group consisting of phenyl, C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, and C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, wherein C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6, substituents independently selected from 0, 1, 2, 3, 4, or 5 halogens, 0 or 1 phenyl, wherein said optional phenyl substituent and said R<sup>930</sup>, when R<sup>930</sup> is phenyl or C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, are optionally substituted with 1, 2, 3, 4, or 5 substituents, independently selected from

halogen, OH, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, or C<sub>5</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, or -OC<sub>5</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, or C<sub>5</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, or -OC<sub>5</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.

wherein R<sup>1025</sup> is selected from R<sup>1030</sup> and hydrogen.

or wherein the group PM

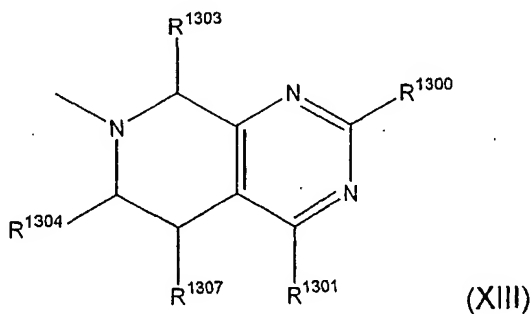
has the formula (XII)



- wherein the groups R<sup>1201</sup> is hydrogen or fluoro.
- wherein R<sup>1200</sup> and A<sup>12</sup> is selected from hydrogen and cyano, and the other is hydrogen.

or wherein the group PM

has the formula XIII:



wherein:

-  $R^{1300}$  is selected from the group consisting of:

- (1) hydrogen,
- (2) CN,
- (3)  $C_{1-10}$ alkyl, which is linear or branched and which is unsubstituted or substituted with:
  - a) halogen, or
  - b) phenyl, which is unsubstituted or substituted with 1 - 5 substituents independently selected from halogen, CN, OH,  $R^{1302}$ ,  $OR^{1302}$ ,  $NHSO_2R^{1302}$ ,  $N(C_{1-6}alkyl)SO_2R^{1302}$ ,  $SO_2R^{1302}$ ,  $SO_2NR^{1305}R^{1306}$ ,  $NR^{1305}R^{1306}$ ,  $CONR^{1305}R^{1306}$ ,  $CO_2H$ , and  $CO_2C_{1-6}alkyl$ , wherein the  $C_{1-6}alkyl$  is linear or branched,
- (4) phenyl which is unsubstituted or substituted with 1 - 5 substituents independently selected from halogen, CN, OH,  $R^{1302}$ ,  $OR^{1302}$ ,  $NHSO_2R^{1302}$ ,  $N(C_{1-6}alkyl)SO_2R^{1302}$ ,  $SO_2R^{1302}$ ,  $SO_2NR^{1305}R^{1306}$ ,  $NR^{1305}R^{1306}$ ,  $CONR^{1305}R^{1306}$ ,  $CO_2H$ , and  $CO_2C_{1-6}alkyl$ , wherein the  $C_{1-6}alkyl$  is linear or branched,
- (5) a 5- or 6-membered heterocyclic which may be saturated or unsaturated comprising 1 - 4 heteroatoms independently selected from N, S and O, the heterocycle being unsubstituted or substituted with 1 - 3 substituents independently selected from oxo, halogen,  $NO_2$ , CN, OH,  $R^{1302}$ ,  $OR^{1302}$ ,  $NHSO_2R^{1302}$ ,  $N(C_{1-6}alkyl)SO_2R^{1302}$ ,  $SO_2R^{1302}$ ,  $SO_2NR^{1305}R^{1306}$ ,  $NR^{1305}R^{1306}$ ,  $CONR^{1305}R^{1306}$ ,  $CO_2H$ , and  $CO_2C_{1-6}alkyl$ , wherein the  $C_{1-6}alkyl$  is linear or branched,
- (6)  $C_{3-6}$ cycloalkyl, which is optionally substituted with 1 - 5 substituents independently selected from halogen, OH,  $C_{1-6}alkyl$ , and  $OC_{1-6}alkyl$ , wherein the  $C_{1-6}alkyl$  and  $OC_{1-6}alkyl$  are linear or branched and optionally substituted with 1 - 5 halogens
- (7) OH
- (8)  $OR^{1302}$ , and
- (9)  $NR^{1305}R^{1306}$ ,

- and  $R^{1301}$  is hydrogen;
- $R^{1302}$  is  $C_{1-6}$ alkyl, which is linear or branched and which is unsubstituted or substituted with 1 – 5 groups independently selected from halogen,  $CO_2H$ , and  $CO_2C_{1-6}$ alkyl, wherein the  $C_{1-6}$ alkyl is linear or branched;
- $R^{1303}$  is selected from the group consisting of:
  - (1) hydrogen,
  - (2)  $C_{1-10}$ alkyl, which is linear or branched and which is unsubstituted or substituted with one or more substituted selected from:
    - a) halogen,
    - b) hydroxy,
    - c) phenyl, which is unsubstituted or substituted with 1 – 5 substituents independently selected from halogen, OH,  $C_{1-6}$ alkyl, and  $OC_{1-6}$ alkyl, wherein the  $C_{1-6}$ alkyl is linear or branched and optionally substituted with 1 – 5 halogens,
    - d) naphthyl, wherein the naphthyl is optionally substituted with 1 – 5 substituents independently selected from halogen, OH,  $C_{1-6}$ alkyl, and  $OC_{1-6}$ alkyl, wherein the  $C_{1-6}$ alkyl is linear or branched and optionally substituted with 1 – 5 halogens,
    - e)  $CO_2H$ ,
    - f)  $CO_2C_{1-6}$ alkyl,
    - g)  $CONR^{1305}R^{1306}$
  - (3) CN,
  - (4) phenyl which is unsubstituted or substituted with 1 – 5 substituents independently selected from  $C_{1-6}$ alkyl, and  $OC_{1-6}$ alkyl, hydroxy and halogen, wherein the  $C_{1-6}$ alkyl is linear or branched and optionally substituted with 1 – 5 halogens,
  - (5) naphthyl which is unsubstituted or substituted with 1 – 5 substituents independently selected from  $C_{1-6}$ alkyl, and  $OC_{1-6}$ alkyl, hydroxy and

halogen, wherein the C<sub>1-6</sub>alkyl is linear or branched and optionally substituted with 1 – 5 halogens,

(6) CO<sub>2</sub>H,

(7) CO<sub>2</sub>C<sub>1-6</sub>alkyl,

(8) CONR<sup>1305</sup>R<sup>1306</sup>, and

(9) C<sub>3-6</sub>cycloalkyl, which is unsubstituted or substituted with 1 – 5 substituents independently selected from C<sub>1-6</sub>alkyl, and OC<sub>1-6</sub>alkyl, hydroxy and halogen, wherein the C<sub>1-6</sub>alkyl is linear or branched and optionally substituted with 1 – 5 halogens

- R<sup>1305</sup> and R<sup>1306</sup> are independently selected from the group consisting of:

(1) hydrogen,

(2) phenyl, which is unsubstituted or substituted with substituents independently selected from halogen, OH, C<sub>1-6</sub>alkyl, and OC<sub>1-6</sub>alkyl, wherein the C<sub>1-6</sub>alkyl is linear or branched and optionally substituted with 1 – 5 halogens

(3) C<sub>3-6</sub>cycloalkyl, which is unsubstituted or substituted with 1 – 5 substituents independently selected from C<sub>1-6</sub>alkyl, and OC<sub>1-6</sub>alkyl, wherein the C<sub>1-6</sub>alkyl is linear or branched and optionally substituted with 1 – 5 halogens

(4) C<sub>1-6</sub>alkyl, which is linear or branched and which is unsubstituted or substituted with:

a) halogen, or

b) phenyl, which is unsubstituted or substituted with 1 – 5 substituents independently selected from halogen, OH, C<sub>1-6</sub>alkyl, and OC<sub>1-6</sub>alkyl, wherein the C<sub>1-6</sub>alkyl is linear or branched and optionally substituted with 1 – 5 halogens,

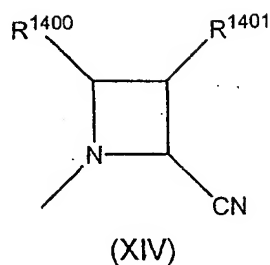
or wherein R<sup>1305</sup> and R<sup>1306</sup> together with the nitrogen atom to which they are attached form a heterocyclic ring selected from azetidine, pyrrolidine, piperidine, piperazine, and morpholine wherein said heterocyclic ring is unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, C<sub>1-6</sub>alkyl, and C<sub>1-</sub>

alkoxy, wherein alkyl and alkoxy are unsubstituted with one to five halogens;

-  $R^{1304}$  and  $R^{1307}$  are hydrogen;

or wherein the group PM

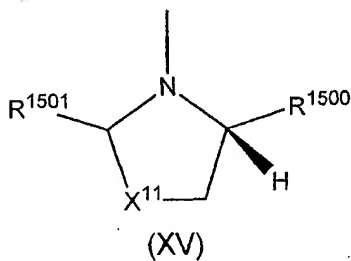
has the formula XIV:



- wherein  $R^{1400}$  is H and  $R^{1401}$  is hydrogen atom (-H); or halogen, or cyano or ethynyl;

or wherein the group PM

has the formula (XV)



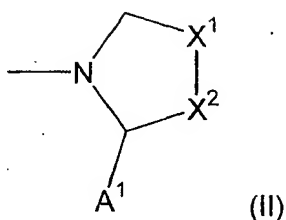
- wherein  $X^{11}$  is  $CH_2$ ,  $CHF$  or  $CF_2$ ;
- wherein  $R^{1500}$  is cyano;
- wherein  $R^{1501}$  is selected from the group consisting of alkyl, alkenyl and alkynyl;



Preferred are compounds as disclosed above

wherein the group **PM**

has the formula (II)



- wherein  $X^1$  is  $CR^{51}R^{52}$  or S; and
- wherein  $X^2$  is  $CR^{54}R^{55}$ ; and

wherein  $R^{51}$ ,  $R^{52}$ ,  $R^{54}$ , and  $R^{55}$ , independently of each other, are a **hydrogen atom** (-H);

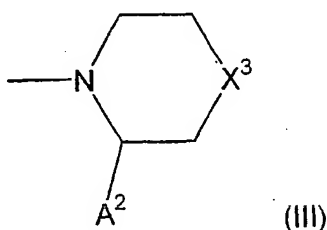
wherein  $A^1$  is

- a **hydrogen atom** (-H), or a **boronic acid** group ( $-B(OH)_2$ ), a **cyano** group ( $-C\equiv N$ ), or a **phosphonic acid ester** group ( $-P(=O)(OR^{116})(OR^{117})$ ),
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the pairs  $R^{116}/R^{117}$  may form a part of a **ring**;
- wherein the substituents  $R^{116}$  and  $R^{117}$  independently of each other, are a **hydrogen atom** (-H), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**,

cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group;

or wherein the group PM

has the formula (III)



wherein  $X^3$  is  $CR^{131}R^{132}$  or S; and

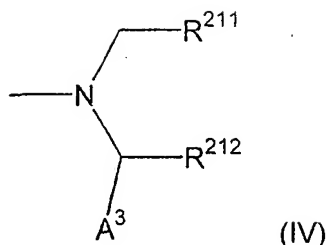
- wherein  $R^{131}$ ,  $R^{132}$ , independently of each other, are a hydrogen atom (-H);

wherein  $A^2$  is

- a hydrogen atom (-H); a boronic acid group ( $-B(OH)_2$ ), a cyano group ( $-C\equiv N$ ), a phosphonic acid ester group ( $-P(=O)(OR^{196})(OR^{197})$ );
- which, independently of each other, can be substituted with one or more substituents, which can be the same or different; and,
- wherein optionally, the pairs  $R^{196}/R^{197}$  may form a part of a ring; and
- wherein the substituents  $R^{196}$  and  $R^{197}$ , independently of each other are a hydrogen atom (-H), or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group;

or wherein the group PM

has the formula (IV)



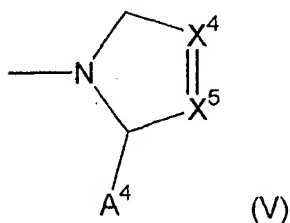
- wherein  $R^{211}$  and  $R^{212}$ , independently of each other, are
- a **hydrogen** atom (-H); or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , and  $C_5$  branched or straight chain **alkyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkenyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkinyl**,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ , and  $C_7$  **cycloalkyl**, **aryl**, **heteroaryl** group or, an **amino** group ( $-NH_2$ ), or a N-substituted or N,N-disubstituted **amino** group ( $-NHR^{240}$ ;  $-NR^{241}R^{242}$ ); and
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the pair  $R^{211}/R^{212}$ , as well the pairs  $R^{226}/R^{227}$ ,  $R^{230}/R^{231}$ ,  $R^{234}/R^{235}$ ,  $R^{236}/R^{237}$  and  $R^{241}/R^{242}$ , independently of each other, may form a part of a **ring**; and
- wherein the substituents  $R^{220}$ ,  $R^{221}$ ,  $R^{222}$ ,  $R^{223}$ ,  $R^{224}$ ,  $R^{225}$ ,  $R^{226}$ ,  $R^{227}$ ,  $R^{228}$ ,  $R^{229}$ ,  $R^{230}$ ,  $R^{231}$ ,  $R^{232}$ ,  $R^{233}$ ,  $R^{234}$ ,  $R^{235}$ ,  $R^{236}$ ,  $R^{237}$ ,  $R^{238}$ ,  $R^{239}$ ,  $R^{240}$ ,  $R^{241}$ , and  $R^{242}$ , independently of each other, are a **hydrogen** atom (-H), or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , and  $C_5$  branched or straight chain **alkyl**, **aryl**, **heteroaryl**, **amino**, **halo**, **carbonyl**,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkoxy**,  $C_2$ ,  $C_3$ ,  $C_4$ ,

C<sub>5</sub> branched or straight chain **alkenoxy, phenyloxy, benzyloxy**, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> **cycloalkyl, cyano, amido, thiol trifluoromethyl, or hydroxy** group; and

- wherein A<sup>3</sup> is
- a **hydrogen** atom (-H); or a **boronic acid** group (-B(OH)<sub>2</sub>), a **cyano** group (-C≡N), or a **phosphonic acid ester** group (-P(=O)(OR<sup>276</sup>)(OR<sup>277</sup>))
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; and,
- wherein optionally, the pair R<sup>276</sup>/R<sup>277</sup> may form a part of a **ring**; and
- wherein the substituents R<sup>276</sup> and R<sup>277</sup>, independently of each other are a **hydrogen** atom (-H), or an **alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl** group;

or wherein the group PM

has the formula (V)



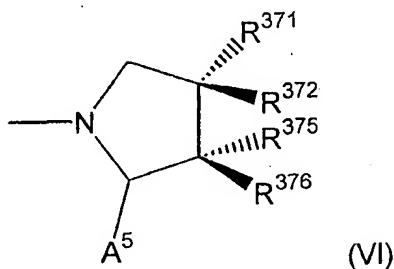
- wherein X<sup>4</sup> is CR<sup>291</sup> or N; and
- wherein X<sup>5</sup> is CR<sup>292</sup> or N; and

- wherein  $R^{291}$  and  $R^{292}$ , independently of each other, are
- a **hydrogen** atom (-H); or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , and  $C_5$  branched or straight chain **alkyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkenyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkinyl**,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ , and  $C_7$  **cycloalkyl**, **aryl**, **heteroaryl** group or an **amino** group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted **amino** group (-NHR<sup>320</sup>, -NR<sup>321</sup>R<sup>322</sup>); and
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the **the pair**  $R^{291}/R^{292}$ , if present, as well the pairs  $R^{306}/R^{307}$ ,  $R^{310}/R^{311}$ ,  $R^{314}/R^{315}$ ,  $R^{316}/R^{317}$  and  $R^{321}/R^{322}$ , independently of each other, may form a part of a **ring**; and
- wherein the substituents  $R^{300}$ ,  $R^{301}$ ,  $R^{302}$ ,  $R^{303}$ ,  $R^{304}$ ,  $R^{305}$ ,  $R^{306}$ ,  $R^{307}$ ,  $R^{308}$ ,  $R^{309}$ ,  $R^{310}$ ,  $R^{311}$ ,  $R^{312}$ ,  $R^{313}$ ,  $R^{314}$ ,  $R^{315}$ ,  $R^{316}$ ,  $R^{317}$ ,  $R^{318}$ ,  $R^{319}$ ,  $R^{320}$ ,  $R^{321}$ , and  $R^{322}$ , independently of each other are a **hydrogen** atom (-H), or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , and  $C_5$  branched or straight chain **alkyl**, **aryl**, **heteroaryl**, **amino**, **halo**, **carbonyl**,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkoxy**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  branched or straight chain **alkenoxy**, **phenyloxy**, **benzyloxy**,  $C_3$ ,  $C_4$ ,  $C_5$  **cycloalkyl**, **cyano**, **amido**, **thiol** **trifluoromethyl**, or **hydroxy** group; and
- wherein  $A^4$  is
- a **hydrogen** atom (-H); or a **boronic acid** group (-B(OH)<sub>2</sub>), a **cyano** group (-C≡N), a **phosphonic acid ester** group (-P(=O)(OR<sup>356</sup>)(OR<sup>357</sup>)),
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the pairs  $R^{356}/R^{357}$  may form a part of a **ring**; and

- wherein the substituents  $R^{356}$  and  $R^{357}$ , independently of each other are a **hydrogen atom (-H)**, or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

or wherein the group PM

has the formula (VI)



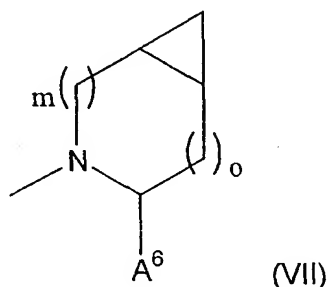
- wherein  $R^{371}$ ,  $R^{372}$ ,  $R^{375}$  and  $R^{376}$ , independently of each other, a **hydrogen atom (-H)**; or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , and  $C_5$  branched or straight chain **alkyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkenyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkinyl**,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ , and  $C_7$  **cycloalkyl**, and **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group or, a **carbaldehyde (-CHO)**, a **ketone group (-CO-R<sup>380</sup>)**, a **boronic acid group (-B(OH)<sub>2</sub>)**, a **cyano group (-C≡N)**, a **carboxylic acid group (-COOH)**, a **carboxylic acid ester group (-COOR<sup>381</sup>)**, a **halogen atom**, a **trifluormethyl group (-CF<sub>3</sub>)**, a **thiol group (-SH)**; a **thioether group (-S-R<sup>398</sup>)**, a **hydroxy group (-OH)**; an **alkoxy group (-O-R<sup>399</sup>)**, a **tetrazole group**, an **amino group (-NH<sub>2</sub>)**, or a **N-substituted or N,N-disubstituted amino group (-NHR<sup>400</sup>; -NR<sup>401</sup>R<sup>402</sup>)**; and
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; and,

- wherein optionally, any two of the groups  $R^{371}$ ,  $R^{372}$ ,  $R^{375}$ , and  $R^{376}$ , as well as the pairs  $R^{386}/R^{387}$ ,  $R^{390}/R^{391}$ ,  $R^{394}/R^{395}$ ,  $R^{396}/R^{397}$  and  $R^{401}/R^{402}$ , independently of each other, may form a part of a **ring**; and
- wherein the substituents  $R^{380}$ ,  $R^{381}$ ,  $R^{382}$ ,  $R^{383}$ ,  $R^{384}$ ,  $R^{385}$ ,  $R^{386}$ ,  $R^{387}$ ,  $R^{388}$ ,  $R^{389}$ ,  $R^{390}$ ,  $R^{391}$ ,  $R^{392}$ ,  $R^{393}$ ,  $R^{394}$ ,  $R^{395}$ ,  $R^{396}$ ,  $R^{397}$ ,  $R^{398}$ ,  $R^{399}$ ,  $R^{400}$ ,  $R^{401}$ , and  $R^{402}$ , independently of each other are a **hydrogen atom (-H)**, or a **C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, and C<sub>5</sub> branched or straight chain alkyl, aryl, heteroaryl, amino, halo, carbonyl, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, branched or straight chain alkoxy, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> branched or straight chain alkenoxy, phenyloxy, benzyloxy, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> cycloalkyl, cyano, amido, thiol trifluoromethyl, or hydroxy group**; and
- alternatively; the two groups  $R^{371}$  and  $R^{372}$  can be together an **oxo (=O)** or **hydroxyimino (=N-OH)** group; and
- alternatively; the two groups  $R^{375}$  and  $R^{376}$  can be together an **oxo (=O)** or **hydroxyimino (=N-OH)** group; and
- wherein **A<sup>5</sup>** is
  - a **hydrogen atom (-H)**; or a **boronic acid group (-B(OH)<sub>2</sub>)**, a **cyano group (-C≡N)**, or a **phosphonic acid ester group (-P(=O)(OR<sup>436</sup>)(OR<sup>437</sup>))**;
  - which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; and,
  - wherein optionally, the pairs  $R^{436}/R^{437}$  may form a part of a **ring**; and
  - wherein the substituents  $R^{436}$  and  $R^{437}$ , independently of each other are a **hydrogen atom (-H)**, or an **alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl,**

heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group;

or wherein the group PM

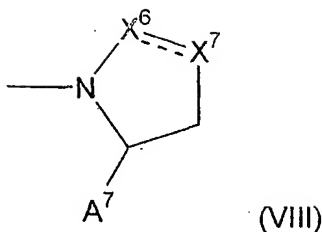
has the formula (VII)



- wherein m is equal to 0 and o is equal to 1, or m is equal to 1 and o is equal to 0, or m is equal to 1 and o is equal to 1, or m is equal to 2 and o is equal to 0;
- wherein  $A^6$  is a **hydrogen** atom (-H); or a **boronic acid** group ( $-B(OH)_2$ ), a **cyano** group ( $-C\equiv N$ ), or a **phosphonic acid ester** group ( $-P(=O)(OR^{476})(OR^{477})$ ),
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the pairs  $R^{476}/R^{477}$  may form a part of a **ring**; and
- wherein the substituents  $R^{476}$  and  $R^{477}$ , independently of each other are a **hydrogen** atom (-H), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;



or wherein the group PM  
has the formula (VIII)



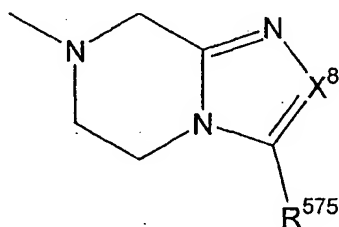
- wherein  $X^6$  is selected from  $CR^{490}R^{491}$ , O, S or  $NR^{492}$ , when the bond between  $X^6$  and  $X^7$  is a single bond; and
- wherein  $X^7$  is selected from  $CR^{493}R^{494}$ , O, S, or  $NR^{495}$ , when the bond between  $X^6$  and  $X^7$  is a single bond;
- **or alternatively,**
- wherein  $X^6$  is selected from  $CR^{496}$  or N, when the bond between  $X^6$  and  $X^7$  is a double bond; and
- wherein  $X^7$  is selected from  $CR^{497}$  or N, when the bond between  $X^6$  and  $X^7$  is a double bond; and
- wherein  $R^{490}$ ,  $R^{491}$ ,  $R^{492}$ ,  $R^{493}$ ,  $R^{494}$ ,  $R^{495}$ ,  $R^{496}$ , and  $R^{497}$ , independently of each other, are a **hydrogen** atom (-H); or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , and  $C_5$  branched or straight chain **alkyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkenyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkinyl**,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ , and  $C_7$  **cycloalkyl**, **aryl**, **heteroaryl** group, or an **amino** group ( $-NH_2$ ), or a N-substituted or N,N-disubstituted **amino** group ( $-NHR^{520}$ ;  $-NR^{521}R^{522}$ ); and
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; and,

- wherein optionally, any two the groups  $R^{490}$ ,  $R^{491}$ ,  $R^{492}$ ,  $R^{493}$ ,  $R^{494}$ ,  $R^{495}$ ,  $R^{496}$ , and  $R^{497}$ , if present, as well as the pairs  $R^{506}/R^{507}$ ,  $R^{510}/R^{511}$ ,  $R^{514}/R^{515}$ ,  $R^{516}/R^{517}$  and  $R^{521}/R^{522}$ , independently of each other, may form a part of a **ring**; and
- wherein the substituents  $R^{500}$ ,  $R^{501}$ ,  $R^{502}$ ,  $R^{503}$ ,  $R^{504}$ ,  $R^{505}$ ,  $R^{506}$ ,  $R^{507}$ ,  $R^{508}$ ,  $R^{509}$ ,  $R^{510}$ ,  $R^{511}$ ,  $R^{512}$ ,  $R^{513}$ ,  $R^{514}$ ,  $R^{515}$ ,  $R^{516}$ ,  $R^{517}$ ,  $R^{518}$ ,  $R^{519}$ ,  $R^{520}$ ,  $R^{521}$ , and  $R^{522}$ , independently of each other are a **hydrogen** atom (-H), or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , and  $C_5$  branched or straight chain **alkyl**, **aryl**, **heteroaryl**, **amino**, **halo**, **carbonyl**,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkoxy**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  branched or straight chain **alkenoxy**, **phenyloxy**, **benzyloxy**,  $C_3$ ,  $C_4$ ,  $C_5$  **cycloalkyl**, **cyano**, **amido**, **thiol** **trifluoromethyl**, or **hydroxy** group; and
- wherein  $A^7$  is
- a **hydrogen** atom (-H); or a **carbaldehyde** (-CHO), a **ketone** group (-CO- $R^{540}$ ), a **boronic acid** group (-B(OH)<sub>2</sub>), a **cyano** group (-C≡N), a **carboxylic acid** group (-COOH), a **carboxylic acid ester** group (-COOR<sup>541</sup>), a **carboxylic acid anhydride** group (-CO-O-CO- $R^{542}$ ), a **hydroxamic acid** group (-CO-NH(OH)), a **N-substituted hydroxamic acid** group (-CO-NR<sup>543</sup>(OH)), a **O-substituted hydroxamic acid** group (-CO-NH(OR<sup>544</sup>)), a **carboxamide** group (-CO-NH<sub>2</sub>), a **N-substituted or N,N-disubstituted carboxylic acid amide** group, (-CO-NHR<sup>545</sup>; -CO-NR<sup>546</sup>R<sup>547</sup>), an **amido** group (-HN-CO- $R^{548}$ ), a **sulfonic acid** group (-SO<sub>3</sub>H), a **sulfonamide** group (-SO<sub>2</sub>-NH<sub>2</sub>), a **N-substituted or N,N-disubstituted sulfonamide** group (-SO<sub>2</sub>-NHR<sup>549</sup>; -SO<sub>2</sub>-NR<sup>550</sup>R<sup>551</sup>), an **amidosulfone** group (-NH-SO<sub>2</sub>-R<sup>552</sup>), a **sulfone** group (-SO<sub>2</sub>-R<sup>553</sup>), a **phosphoric acid** group (-OP(=O)(OH)<sub>2</sub>), a **phosphoric acid ester** group (-OP(=O)(OR<sup>554</sup>)(OR<sup>555</sup>)), a **phosphonic acid** group (-P(=O)(OH)<sub>2</sub>), an **phosphonic acid ester** group (-P(=O)(OR<sup>556</sup>)(OR<sup>557</sup>)), a **halogen atom**, a **trifluormethyl** group (-CF<sub>3</sub>), a **thiol** group (-SH); a **thioether** group (-S-R<sup>558</sup>), a **hydroxy** group (-OH); an **alkoxy** group (-O-R<sup>559</sup>), a **tetrazole** group, an **amino** group (-NH<sub>2</sub>), or a **N-substituted or N,N-disubstituted amino** group (-NHR<sup>560</sup>; -NR<sup>561</sup>R<sup>562</sup>); and

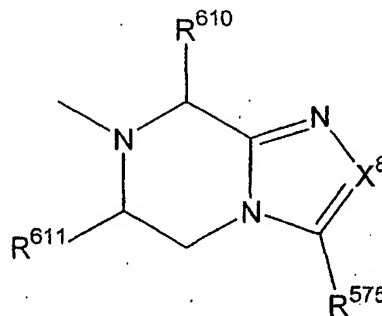
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the pairs  $R^{546}/R^{547}$ ,  $R^{550}/R^{551}$ ,  $R^{554}/R^{555}$ ,  $R^{556}/R^{557}$  and  $R^{561}/R^{562}$ , independently of each other, may form a part of a **ring**; **and**
- wherein the substituents  $R^{540}$ ,  $R^{541}$ ,  $R^{542}$ ,  $R^{543}$ ,  $R^{544}$ ,  $R^{545}$ ,  $R^{546}$ ,  $R^{547}$ ,  $R^{548}$ ,  $R^{549}$ ,  $R^{550}$ ,  $R^{551}$ ,  $R^{552}$ ,  $R^{553}$ ,  $R^{554}$ ,  $R^{555}$ ,  $R^{556}$ ,  $R^{557}$ ,  $R^{558}$ ,  $R^{559}$ ,  $R^{560}$ ,  $R^{561}$ , and  $R^{562}$ , independently of each other are a **hydrogen** atom (-H), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

or wherein the group **PM**

has the formula (IX) or (IXa)



(IX)



(IXa)

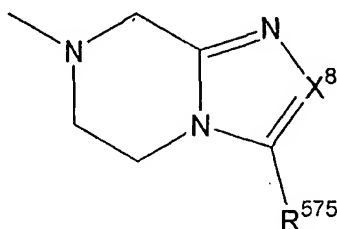
- wherein  $X^8$  is N or  $CR^{570}$ ; **and**
- wherein  $R^{570}$ ,  $R^{575}$ ,  $R^{610}$  and  $R^{611}$  independently of each other, are
- a **hydrogen** atom (-H), a **methyl** group (-CH<sub>3</sub>), a **trifluoromethyl** group (-CF<sub>3</sub>), an **ethyl** group (-C<sub>2</sub>H<sub>5</sub>), a **2,2,2-trifluoroethyl** group (-CH<sub>2</sub>CF<sub>3</sub>), a **pentafluoroethyl** group (-CF<sub>2</sub>CF<sub>3</sub>), a **phenyl** group, (-C<sub>6</sub>H<sub>5</sub>), a **benzyl** group

(-CH<sub>2</sub>-C<sub>6</sub>H<sub>5</sub>), a **benzyloxy** group (-OCH<sub>2</sub>-C<sub>6</sub>H<sub>5</sub>), a **para-ethyl-phenyl** group (-C<sub>6</sub>H<sub>4</sub>-C<sub>2</sub>H<sub>5</sub>), a **para-fluorophenyl** group (-C<sub>6</sub>H<sub>4</sub>-4-F), a **3,4-difluorophenyl** group (-C<sub>6</sub>H<sub>3</sub>-3,4-F<sub>2</sub>), a **para-methoxyphenyl** group (-C<sub>6</sub>H<sub>4</sub>-4-OCH<sub>3</sub>), a **para-trifluoromethoxyphenyl** group (-C<sub>6</sub>H<sub>4</sub>-4-OCF<sub>3</sub>), a **boronic acid** group (-B(OH)<sub>2</sub>), a **cyano** group (-C≡N), a **carboxylic acid** group (-COOH), or a **phosphonic acid ester** group (-P(=O)(OR<sup>596</sup>)(OR<sup>597</sup>));

- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the pairs R<sup>570</sup>/R<sup>575</sup>, if present, as well as the pair R<sup>596</sup>/R<sup>597</sup>, independently of each other, may form a part of a **ring**; and
- wherein the substituents R<sup>596</sup> and R<sup>597</sup>, independently of each other are a **hydrogen** atom (-H), or a C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, and C<sub>5</sub> branched or straight chain **alkyl**, **aryl**, **heteroaryl**, **amino**, **halo**, **carbonyl**, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, branched or straight chain **alkoxy**, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> branched or straight chain **alkenoxy**, **phenyloxy**, **benzyloxy**, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> **cycloalkyl**, **cyano**, **amido**, **thiol** **trifluoromethyl**, or **hydroxy** group; and

or wherein the group PM

has the formula (IX)



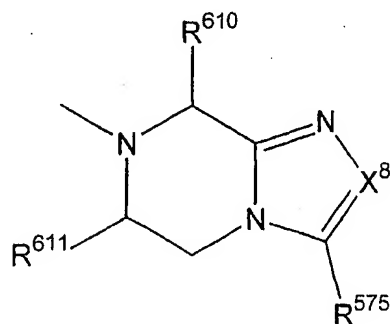
(IX)

- wherein X<sup>8</sup> is N or CR<sup>570</sup>; and

- wherein  $R^{570}$  and  $R^{575}$ , independently of each other, are
  - (1) hydrogen,
  - (2) CN,
  - (3)  $C_{1-10}$  alkyl, which is linear or branched and which is unsubstituted or substituted with 1-5 halogens or phenyl, which is unsubstituted or substituted with 1-5 substituents independently selected from halogen, CN, OH,  $R^{612}$ ,  $OR^{612}$ ,  $NHSO_2R^{612}$ ,  $SO_2R^{612}$ ,  $CO_2H$ , and  $CO_2C_{1-6}$  alkyl, wherein the  $CO_2C_{1-6}$  alkyl is linear or branched,
  - (4) phenyl which is unsubstituted or substituted with 1-5 substituents independently selected from halogen, CN, OH,  $R^{612}$ ,  $OR^{612}$ ,  $NHSO_2R^{612}$ ,  $SO_2R^{612}$ ,  $CO_2H$ , and  $CO_2C_{1-6}$  alkyl, wherein the  $CO_2C_{1-6}$  alkyl is linear or branched, and
  - (5) a 5- or 6-membered heterocycle which may be saturated or unsaturated comprising 1-4 heteroatoms independently selected from N, S, and O, the heterocycle being unsubstituted or substituted with 1-3 substituents independently selected from oxo, OH, halogen,  $C_{1-6}$  alkyl, and  $OC_{1-6}$  alkyl, wherein  $C_{1-6}$  alkyl and  $C_{1-6}$  alkoxy are linear or branched and optionally substituted with 1-5 halogens, and
- wherein  $R^{612}$  is  $C_{1-6}$  alkyl, which is linear or branched and which is unsubstituted or substituted with 1-5 groups independently selected from halogen,  $CO_2H$ , and  $CO_2C_{1-6}$  alkyl, wherein the  $CO_2C_{1-6}$  alkyl is linear or branched.

or wherein the group PM

has the formula (IXa)



(IXa)

- wherein  $X^8$  is N or  $CR^{570}$ ; and
- wherein  $R^{570}$  and  $R^{575}$  independently of each other, are
  - (6) hydrogen,
  - (7) CN,
  - (8)  $C_{1-10}$  alkyl, which is linear or branched and which is unsubstituted or substituted with 1-5 halogens or phenyl, which is unsubstituted or substituted with 1-5 substituents independently selected from halogen, CN, OH,  $R^{612}$ ,  $OR^{612}$ ,  $NHSO_2R^{612}$ ,  $SO_2R^{612}$ ,  $CO_2H$ , and  $CO_2C_{1-6}$  alkyl, wherein the  $CO_2C_{1-6}$  alkyl is linear or branched,
  - (9) phenyl which is unsubstituted or substituted with 1-5 substituents independently selected from halogen, CN, OH,  $R^{612}$ ,  $OR^{612}$ ,  $NHSO_2R^{612}$ ,  $SO_2R^{612}$ ,  $CO_2H$ , and  $CO_2C_{1-6}$  alkyl, wherein the  $CO_2C_{1-6}$  alkyl is linear or branched, and
  - (10) a 5- or 6-membered heterocycle which may be saturated or unsaturated comprising 1-4 heteroatoms independently selected from N, S, and O, the heterocycle being unsubstituted or substituted with 1-3 substituents independently selected from oxo, OH, halogen,  $C_{1-6}$  alkyl, and  $OC_{1-6}$  alkyl, wherein  $C_{1-6}$  alkyl and  $C_{1-6}$  alkoxy are linear or branched and optionally substituted with 1-5 halogens, and
- wherein  $R^{612}$  is  $C_{1-6}$  alkyl, which is linear or branched and which is unsubstituted or substituted with 1-5 groups independently selected from halogen,  $CO_2H$ , and  $CO_2C_{1-6}$  alkyl, wherein the  $CO_2C_{1-6}$  alkyl is linear or branched, and
- wherein  $R^{610}$  and  $R^{611}$  are each independently selected from the group consisting of
  - (1) hydrogen,
  - (2)  $C_{1-10}$  alkyl, which is linear or branched and which is unsubstituted or substituted with one or more substituents selected from:
    - (a) halogen,
    - (b) hydroxy,
    - (c) phenyl, wherein the phenyl is unsubstituted or substituted with 1-5 substituents independently selected from halogen, OH,  $C_{1-6}$  alkyl,

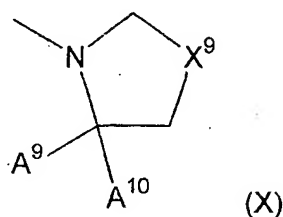
- and C<sub>1-6</sub> alkoxy, wherein the C<sub>1-6</sub> alkyl, and C<sub>1-6</sub> alkoxy are linear or branched and optionally substituted with 1-5 halogens,
- (d) naphthyl, wherein the naphthyl is optionally substituted with 1-5 substituents independently selected from halogen, CN, OH, C<sub>1-6</sub> alkyl, and C<sub>1-6</sub> alkoxy, wherein the C<sub>1-6</sub> alkyl, and C<sub>1-6</sub> alkoxy are linear or branched and optionally substituted with 1-5 halogens,
- (e) CO<sub>2</sub>H,
- (f) CO<sub>2</sub>C<sub>1-6</sub> alkyl,
- (g) CONR<sup>613</sup>R<sup>614</sup>, wherein R<sup>613</sup> and R<sup>614</sup> are independently selected from the group consisting of hydrogen, tetrazolyl, phenyl, C<sub>3-6</sub> cycloalkyl and C<sub>1-6</sub> alkyl, wherein the C<sub>1-6</sub> alkyl is linear or branched and is optionally substituted with 1-6 substituents independently selected from 0-5 halogen and 0-1 phenyl, wherein the phenyl or the C<sub>3-6</sub> cycloalkyl bearing R<sup>613</sup> and R<sup>614</sup> or the optional phenyl substituent on the C<sub>1-6</sub> alkyl are optionally substituted with 1-5 substituents independently selected from halogen, OH, C<sub>1-6</sub> alkyl, and OC<sub>1-6</sub> alkyl, said C<sub>1-6</sub> alkyl and OC<sub>1-6</sub> alkyl being linear or branched and optionally substituted with 1-5 halogens,
- or wherein R<sup>613</sup> and R<sup>614</sup> are optionally joined to form a ring selected from pyrrolidine, piperidine or morpholine,
- (3) CN,
- (4) phenyl, wherein the phenyl is unsubstituted or substituted with 1-5 substituents independently selected from C<sub>1-6</sub> alkyl, and C<sub>1-6</sub> alkoxy, hydroxy and halogen, wherein the C<sub>1-6</sub> alkyl, and C<sub>1-6</sub> alkoxy are linear or branched and optionally substituted with 1-5 halogens,
- (5) naphthyl, wherein the naphthyl is unsubstituted or substituted with 1-5 substituents independently selected from halogen, OH, C<sub>1-6</sub> alkyl, and C<sub>1-6</sub> alkoxy, wherein the C<sub>1-6</sub> alkyl, and C<sub>1-6</sub> alkoxy are linear or branched and optionally substituted with 1-5 halogens,
- (6) CO<sub>2</sub>H,
- (7) CO<sub>2</sub>C<sub>1-6</sub> alkyl,

(8)  $\text{CONR}^{613}\text{R}^{614}$ , and

(9)  $\text{C}_{3-6}$  cycloalkyl, which is optionally substituted with 1-5 substituents independently selected from halogen, OH,  $\text{C}_{1-6}$  alkyl, and  $\text{C}_{1-6}$  alkoxy, wherein the  $\text{C}_{1-6}$  alkyl, and  $\text{C}_{1-6}$  alkoxy are linear or branched and optionally substituted with 1-5 halogen, with the proviso that one of  $\text{R}^{610}$  and  $\text{R}^{611}$  is other than hydrogen.

or wherein the group PM

has the formula (X)



- wherein the groups  $\text{X}^9$  is  $\text{CR}^{900}\text{R}^{901}$ , S,  $\text{SO}$ ,  $\text{SO}_2$  or  $\text{NR}^{902}$ 
  - wherein  $\text{R}^{900}$ ,  $\text{R}^{901}$  and  $\text{R}^{902}$ , are, independently of each other, selected from hydrogen, fluorine,  $\text{C}_1$ ,  $\text{C}_2$ ,  $\text{C}_3$ ,  $\text{C}_4$ ,  $\text{C}_5$  or  $\text{C}_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens, or  $-\text{C}(=\text{O})\text{NR}^{910}\text{R}^{911}$ .
- wherein  $\text{A}^9$  and  $\text{A}^{10}$  are, independently of each other, selected from hydrogen, cyano,  $-\text{C}(=\text{O})\text{NR}^{912}\text{R}^{913}$ , or  $\text{C}_1$ ,  $\text{C}_2$ ,  $\text{C}_3$ ,  $\text{C}_4$ ,  $\text{C}_5$  or  $\text{C}_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein

- $\text{R}^{910}$  and  $\text{R}^{912}$ , are, independently of each other, selected from hydrogen, or  $\text{C}_1$ ,  $\text{C}_2$ ,  $\text{C}_3$ ,  $\text{C}_4$ ,  $\text{C}_5$  or  $\text{C}_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens; and



- $R^{911}$  and  $R^{913}$ , are, independently of each other, selected from the group consisting of

(1) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5, substituents independently selected from halogen and  $R^{920}$ ;

(2)  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6 or 7 substituents independently selected from (a) 0, 1, 2, 3, 4, or 5 halogens, and (b) 0, 1, 2 substituents selected from the group consisting of

- (a) hydroxy,
- (b)  $-COOH$ ,
- (c)  $-COO(C_1, C_2, C_3, C_4, C_5 \text{ or } C_6 \text{ alkyl})$ , i.e. ester,
- (d) phenyl,
- (e) naphthyl,
- (f)  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  cycloalkyl,
- (g) a 5 - or 6 membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur;
- (h) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (a) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (b) a benzene ring fused to a 5- or 6-membered heterocycle having 1, 2, or 3 hetero atoms;

- wherein said  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  cycloalkyl, phenyl, naphthyl, are optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from halogen and  $R^{920}$ , and said 5 or 6 membered heterocycle and said 8, 9 or 10 - membered bicyclic ring system are each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, and  $R^{920}$ ; and

(3) C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, which is optionally substituted with 1, 2, or 3 groups independently selected from halogen, hydroxy, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein R<sup>920</sup> is selected from the group consisting of:

(1) hydroxy;

(2) cyano;

(3) C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl optionally substituted with 1, 2, or 3 groups independently selected from halogen, hydroxy, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, wherein said -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl are linear or branched and are optionally substituted with 1, 2, 3, 4, 5 or 6 substituents selected from 1, 2, 3, 4, or 5 halogens, and 0 or 1 substituents selected from -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, -COOH, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl substituents being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(4) C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub>, C<sub>9</sub> or C<sub>10</sub> alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6, or 7 substituents independently selected from 0, 1, 2, 3, 4, or 5 halogen atoms and 0, 1, or 2 groups selected from

(a) hydroxy;

(b) -COOH;

(c) -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, which may linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens;

(d) a 5 - or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, optionally substituted with 1, 2, or 3

substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.;

(e) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (i) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (ii) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(f) -CONR<sup>925</sup>R<sup>925</sup>;

(g) -SO<sub>2</sub>NR<sup>925</sup>R<sup>925</sup>;

(h) -NR<sup>925</sup>-C(=O)R<sup>925</sup>

(i) -NR<sup>925</sup>-C(=O)NR<sup>925</sup>R<sup>925</sup>;

(j) -NR<sup>925</sup>COOR<sup>930</sup>

(k) -O-CO-R<sup>930</sup>

(l) -O-CO-NR<sup>925</sup>R<sup>925</sup>;

(m) -NR<sup>925</sup>SO<sub>2</sub>R<sup>930</sup>;

(n) -NR<sup>925</sup>R<sup>925</sup>;

(o) phenyl which is optionally substituted with 1, 2, 3, 4, or 5 group independently selected from halogen, hydroxy, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester being linear or branched and optionally substituted

with 1, 2, 3, 4, 5, or 6 substituents independently selected from 0 or 1

C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl and 0, 1, 2, 3, 4, or 5 halogens, and

(p) C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, which is optionally substituted with 1, 2, 3, 4, 5, or 6 halogens;

(5) OC<sub>1</sub>, OC<sub>2</sub>, OC<sub>3</sub>, OC<sub>4</sub>, OC<sub>5</sub>, OC<sub>6</sub>, OC<sub>7</sub>, OC<sub>8</sub>, OC<sub>9</sub> or OC<sub>10</sub> alkyl, which is linear or branched and is optionally substituted with 0, 1, 2, 3, 4, or 5 halogen atoms and 0, 1, or 2 substituents selected from

(a) hydroxy;

(b)-COOH;

(c) -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, which may be linear or branched and is optionally substituted with 1, 2, 3, 4 or 5 halogens;

(d) a 5 - or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.;

(e) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (i) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (ii) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(f) -CONR<sup>925</sup>R<sup>925</sup>;

- (g)  $-\text{SO}_2\text{NR}^{925}\text{R}^{925}$ ;
- (h)  $-\text{NR}^{925}-\text{C}(=\text{O})\text{R}^{925}$
- (i)  $-\text{NR}^{925}-\text{C}(=\text{O})\text{NR}^{925}\text{R}^{925}$ ;
- (j)  $-\text{NR}^{925}\text{COOR}^{930}$
- (k)  $-\text{O}-\text{CO}-\text{R}^{930}$
- (l)  $-\text{O}-\text{CO}-\text{NR}^{925}\text{R}^{925}$ ;
- (m)  $-\text{NR}^{925}\text{SO}_2\text{R}^{930}$ ;
- (n)  $-\text{NR}^{925}\text{R}^{925}$ ;

(o) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5 groups independently selected from halogen, hydroxy,  $\text{C}_1$ ,  $\text{C}_2$ ,  $\text{C}_3$ ,  $\text{C}_4$ ,  $\text{C}_5$  or  $\text{C}_6$  alkyl,  $-\text{OC}_1$ ,  $-\text{OC}_2$ ,  $-\text{OC}_3$ ,  $-\text{OC}_4$ ,  $-\text{OC}_5$  or  $-\text{OC}_6$  alkyl,  $-\text{COOH}$ ,  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester, said  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  alkyl,  $-\text{OC}_1$ ,  $-\text{OC}_2$ ,  $-\text{OC}_3$ ,  $-\text{OC}_4$ ,  $-\text{OC}_5$  or  $-\text{OC}_6$  alkyl,  $-\text{COOH}$ ,  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, 5, or 6 substituents independently selected from 0 or 1  $\text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  cycloalkyl and 0, 1, 2, 3, 4, or 5 halogens, and

(p)  $\text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  cycloalkyl, which is optionally substituted with 1, 2, 3, 4, 5, or 6 halogens;

- (6)  $-\text{COOH}$ ;
- (7)  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester, which may be linear or branched and is optionally substituted with 1, 2, 3, 4, 5 halogens;
- (8) a 5- or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, said heterocycle being optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen,  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5$  or  $-\text{OC}_6$  alkyl, said  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5$  or  $-\text{OC}_6$  alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.
- (9) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (a) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen,

oxygen or sulfur, or (b) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(10) -CONR<sup>925</sup>R<sup>925</sup>;

(11) -SO<sub>2</sub>NR<sup>925</sup>R<sup>925</sup>;

(12) -NR<sup>925</sup>-C(=O)R<sup>925</sup>

(13) -NR<sup>925</sup>-C(=O)NR<sup>925</sup>R<sup>925</sup>;

(14) -NR<sup>925</sup>COOR<sup>930</sup>

(15) -O-CO-R<sup>930</sup>

(16) -O-CO-NR<sup>925</sup>R<sup>925</sup>;

(17) -NR<sup>925</sup>SO<sub>2</sub>R<sup>930</sup>;

(18) -NR<sup>925</sup>R<sup>925</sup>;

(19) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5 group independently selected from halogen, hydroxy, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

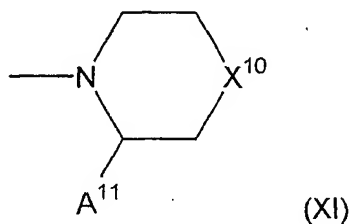
wherein R<sup>930</sup> is selected from the group consisting of phenyl, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl, and C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl, wherein C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6, substituents independently selected from 0, 1, 2, 3, 4, or 5 halogens, 0 or 1 phenyl, wherein said optional phenyl substituent and said R<sup>930</sup>, when R<sup>930</sup> is phenyl or C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl, are optionally substituted with 1, 2, 3, 4, or 5 substituents, independently selected from

halogen, OH, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, or C<sub>5</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, or -OC<sub>5</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, or C<sub>5</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, or -OC<sub>5</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.

wherein R<sup>925</sup> is selected from R<sup>930</sup> and hydrogen.

wherein the group PM

has the formula (XI)



- wherein the groups X<sup>10</sup> is CR<sup>1000</sup>R<sup>1001</sup>, S, SO, SO<sub>2</sub> or NR<sup>1002</sup>
- wherein R<sup>1000</sup>, R<sup>1001</sup> and R<sup>1002</sup>, are, independently of each other, selected from hydrogen, fluorine, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens, or -C(=O)NR<sup>1010</sup>R<sup>1011</sup>.

and A<sup>11</sup> is selected from

hydrogen, cyano, -C(=O)NR<sup>1012</sup>R<sup>1013</sup>, or C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein

- R<sup>1010</sup> and R<sup>1012</sup>, are, independently of each other, selected from hydrogen, or C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens; and
- R<sup>1011</sup> and R<sup>1013</sup>, are, independently of each other, selected from the group consisting of

(1) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5, substituents independently selected from halogen and  $R^{1020}$ ;

(2)  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6 or 7 substituents independently selected from (a) 0, 1, 2, 3, 4, or 5 halogens, and (b) 0, 1, 2 substituents selected from the group consisting of

- (a) hydroxy,
- (b)  $-COOH$ ,
- (c)  $-COO(C_1, C_2, C_3, C_4, C_5$  or  $C_6$  alkyl), i.e. ester,
- (d) phenyl,
- (e) naphthyl,
- (f)  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  cycloalkyl,
- (g) a 5 - or 6 membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur;
- (h) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (a) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (b) a benzene ring fused to a 5- or 6-membered heterocycle having 1, 2, or 3 hetero atoms;

- wherein said  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  cycloalkyl, phenyl, naphthyl, are optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from halogen and  $R^{1020}$ , and said 5 or 6 membered heterocycle and said 8, 9 or 10 - membered bicyclic ring system are each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, and  $R^{1020}$ ; and

(3)  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  cycloalkyl, which is optionally substituted with 1, 2, or 3 groups independently selected from halogen, hydroxy,  $-COOH$ ,  $-COO(C_1, C_2,$



C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein R<sup>1020</sup> is selected from the group consisting of:

- (1) hydroxy;
- (2) cyano;
- (3) C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl optionally substituted with 1, 2, or 3 groups independently selected from halogen, hydroxy, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, wherein said -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl are linear or branched and are optionally substituted with 1, 2, 3, 4, 5 or 6 substituents selected from 1, 2, 3, 4, or 5 halogens, and 0 or 1 substituents selected from -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, -COOH, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl substituents being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;
- (4) C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub>, C<sub>9</sub> or C<sub>10</sub> alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6, or 7 substituents independently selected from 0, 1, 2, 3, 4, or 5 halogen atoms and 0, 1, or 2 groups selected from
  - (a) hydroxy;
  - (b) -COOH;
  - (c) -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, which may linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens;
  - (d) a 5- or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl,

said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(e) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (i) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (ii) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(f) -CONR<sup>1025</sup>R<sup>1025</sup>;

(g) -SO<sub>2</sub>NR<sup>1025</sup>R<sup>1025</sup>;

(h) -NR<sup>1025</sup>-C(=O)R<sup>1025</sup>

(i) -NR<sup>1025</sup>-C(=O)NR<sup>1025</sup>R<sup>1025</sup>;

(j) -NR<sup>1025</sup>COOR<sup>1030</sup>

(k) -O-CO-R<sup>1030</sup>

(l) -O-CO-NR<sup>1025</sup>R<sup>1025</sup>;

(m) -NR<sup>1025</sup>SO<sub>2</sub>R<sup>1030</sup>;

(n) -NR<sup>1025</sup>R<sup>1025</sup>;

(o) phenyl which is optionally substituted with 1, 2, 3, 4, or 5 group independently selected from halogen, hydroxy, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, 5, or 6 substituents independently selected from 0 or 1 C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl and 0, 1, 2, 3, 4, or 5 halogens, and

- (p) C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl, which is optionally substituted with 1, 2, 3, 4, 5, or 6 halogens;
- (5) OC<sub>1</sub>, OC<sub>2</sub>, OC<sub>3</sub>, OC<sub>4</sub>, OC<sub>5</sub>, OC<sub>6</sub>, OC<sub>7</sub>, OC<sub>8</sub>, OC<sub>9</sub> or OC<sub>10</sub> alkyl, which is linear or branched and is optionally substituted with 0, 1, 2, 3, 4, or 5 halogen atoms and 0, 1, or 2 substituents selected from
- (a) hydroxy;
  - (b) -COOH;
  - (c) -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, which may be linear or branched and is optionally substituted with 1, 2, 3, 4 or 5 halogens;
  - (d) a 5- or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.;
  - (e) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (i) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (ii) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;
  - (f) -CONR<sup>1025</sup>R<sup>1025</sup>;
  - (g) -SO<sub>2</sub>NR<sup>1025</sup>R<sup>1025</sup>;
  - (h) -NR<sup>1025</sup>-C(=O)R<sup>1025</sup>

(i)  $-\text{NR}^{1025}-\text{C}(=\text{O})\text{NR}^{1025}\text{R}^{1025}$ ;

(j)  $-\text{NR}^{1025}\text{COOR}^{1030}$

(k)  $-\text{O}-\text{CO}-\text{R}^{1030}$

(l)  $-\text{O}-\text{CO}-\text{NR}^{1025}\text{R}^{1025}$ ;

(m)  $-\text{NR}^{1025}\text{SO}_2\text{R}^{1030}$ ;

(n)  $-\text{NR}^{1025}\text{R}^{1025}$ ;

(o) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5 groups independently selected from halogen, hydroxy,  $\text{C}_1$ ,  $\text{C}_2$ ,  $\text{C}_3$ ,  $\text{C}_4$ ,  $\text{C}_5$  or  $\text{C}_6$  alkyl,  $-\text{OC}_1$ ,  $-\text{OC}_2$ ,  $-\text{OC}_3$ ,  $-\text{OC}_4$ ,  $-\text{OC}_5$  or  $-\text{OC}_6$  alkyl,  $-\text{COOH}$ ,  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester, said  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  alkyl,  $-\text{OC}_1$ ,  $-\text{OC}_2$ ,  $-\text{OC}_3$ ,  $-\text{OC}_4$ ,  $-\text{OC}_5$  or  $-\text{OC}_6$  alkyl,  $-\text{COOH}$ ,  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, 5, or 6 substituents independently selected from 0 or 1  $\text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  cycloalkyl and 0, 1, 2, 3, 4, or 5 halogens, and

(p)  $\text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  cycloalkyl, which is optionally substituted with 1, 2, 3, 4, 5, or 6 halogens;

(6)  $-\text{COOH}$ ;

(7)  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester, which may be linear or branched and is optionally substituted with 1, 2, 3, 4, 5 halogens;

(8) a 5- or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, said heterocycle being optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen,  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5$  or  $-\text{OC}_6$  alkyl, said  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5$  or  $-\text{OC}_6$  alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.

(9) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (a) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (b) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused

to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(10) -CONR<sup>1025</sup>R<sup>1025</sup>;

(11) -SO<sub>2</sub>NR<sup>1025</sup>R<sup>1025</sup>;

(12) -NR<sup>1025</sup>-C(=O)R<sup>1025</sup>

(13) -NR<sup>1025</sup>-C(=O)NR<sup>1025</sup>R<sup>1025</sup>;

(14) -NR<sup>925</sup>COOR<sup>1030</sup>

(15) -O-CO-R<sup>1030</sup>

(16) -O-CO-NR<sup>1025</sup>R<sup>1025</sup>;

(17) -NR<sup>1025</sup>SO<sub>2</sub>R<sup>1030</sup>;

(18) - NR<sup>1025</sup>R<sup>1025</sup>;

(19) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5 group independently selected from halogen, hydroxy, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

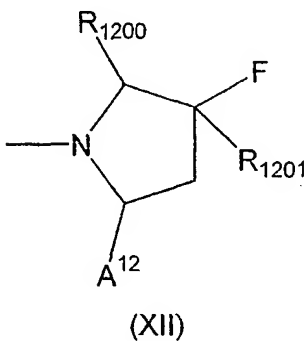
wherein R<sup>1030</sup> is selected from the group consisting of phenyl, C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, and C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, wherein C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6, substituents independently selected from 0, 1, 2, 3, 4, or 5 halogens, 0 or 1 phenyl, wherein said optional phenyl substituent and said R<sup>930</sup>, when R<sup>930</sup> is phenyl or C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, are optionally substituted with 1, 2, 3, 4, or 5 substituents, independently selected from halogen, OH, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, or C<sub>5</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, or -OC<sub>5</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, or C<sub>5</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, or -OC<sub>5</sub>

alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens,

wherein  $R^{1025}$  is selected from  $R^{1030}$  and hydrogen.

or wherein the group PM

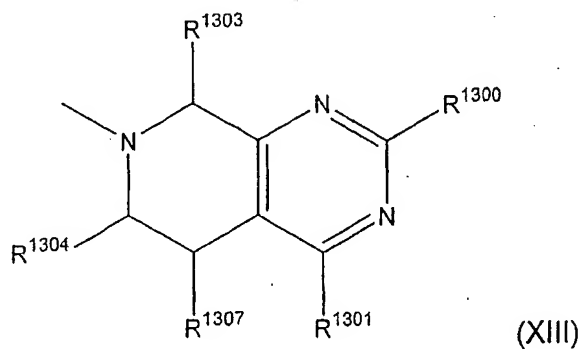
has the formula (XII)



- wherein the groups  $R^{1201}$  is hydrogen or fluoro.
- wherein  $R^{1200}$  and  $A^{12}$  is selected from hydrogen and cyano, and the other is hydrogen.

or wherein the group PM

has the formula XIII:



wherein:

-  $R^{1300}$  is selected from the group consisting of:

- (1) hydrogen,
- (2) CN,
- (3)  $C_{1-10}$ alkyl, which is linear or branched which is unsubstituted or substituted with:
  - a) halogen, or
  - b) phenyl, which is unsubstituted or substituted with 1 - 5 substituents independently selected from halogen, CN, OH,  $R^{1302}$ ,  $OR^{1302}$ ,  $NHSO_2R^{1302}$ ,  $N(C_{1-6}alkyl)SO_2R^{1302}$ ,  $SO_2R^{1302}$ ,  $SO_2NR^{1305}R^{1306}$ ,  $NR^{1305}R^{1306}$ ,  $CONR^{1305}R^{1306}$ ,  $CO_2H$ , and  $CO_2C_{1-6}alkyl$ , wherein the  $C_{1-6}alkyl$  is linear or branched,
- (4) phenyl which is unsubstituted or substituted with 1 - 5 substituents independently selected from halogen, CN, OH,  $R^{1302}$ ,  $OR^{1302}$ ,  $NHSO_2R^{1302}$ ,  $N(C_{1-6}alkyl)SO_2R^{1302}$ ,  $SO_2R^{1302}$ ,  $SO_2NR^{1305}R^{1306}$ ,  $NR^{1305}R^{1306}$ ,  $CONR^{1305}R^{1306}$ ,  $CO_2H$ , and  $CO_2C_{1-6}alkyl$ , wherein the  $C_{1-6}alkyl$  is linear or branched,
- (5) a 5- or 6-membered heterocyclic which may be saturated or unsaturated comprising 1 - 4 heteroatoms independently selected from N, S and O, the heterocycle being unsubstituted or substituted with 1 - 3 substituents independently selected from oxo, halogen,  $NO_2$ , CN, OH,  $R^{1302}$ ,  $OR^{1302}$ ,  $NHSO_2R^{1302}$ ,  $N(C_{1-6}alkyl)SO_2R^{1302}$ ,  $SO_2R^{1302}$ ,  $SO_2NR^{1305}R^{1306}$ ,  $NR^{1305}R^{1306}$ ,  $CONR^{1305}R^{1306}$ ,  $CO_2H$ , and  $CO_2C_{1-6}alkyl$ , wherein the  $C_{1-6}alkyl$  is linear or branched,
- (6)  $C_{3-6}$ cycloalkyl, which is optionally substituted with 1 - 5 substituents independently selected from halogen, OH,  $C_{1-6}alkyl$ , and  $OC_{1-6}alkyl$ , wherein the  $C_{1-6}alkyl$  and  $OC_{1-6}alkyl$  are linear or branched and optionally substituted with 1 - 5 halogens,
- (7) OH,
- (8)  $OR^{1302}$ , and

(9)  $\text{NR}^{1305}\text{R}^{1306}$ ;

-  $\text{R}^{1301}$  is hydrogen;

-  $\text{R}^{1302}$  is  $\text{C}_{1-6}$ alkyl, which is linear or branched and which is unsubstituted or substituted with 1 – 5 groups independently selected from halogen,  $\text{CO}_2\text{H}$ , and  $\text{CO}_2\text{C}_{1-6}$ alkyl, wherein the  $\text{C}_{1-6}$ alkyl is linear or branched;

-  $\text{R}^{1303}$  is hydrogen;

-  $\text{R}^{1305}$  and  $\text{R}^{1306}$  are independently selected from the group consisting of:

(1) hydrogen,

(2) phenyl, which is unsubstituted or substituted with substituents independently selected from halogen, OH,  $\text{C}_{1-6}$ alkyl, and  $\text{OC}_{1-6}$ alkyl, wherein the  $\text{C}_{1-6}$ alkyl is linear or branched and optionally substituted with 1 – 5 halogens

(3)  $\text{C}_{3-6}$ cycloalkyl, which is unsubstituted or substituted with 1 – 5 substituents independently selected from  $\text{C}_{1-6}$ alkyl, and  $\text{OC}_{1-6}$ alkyl, wherein the  $\text{C}_{1-6}$ alkyl is linear or branched and optionally substituted with 1 – 5 halogens

(4)  $\text{C}_{1-6}$ alkyl, which is linear or branched and which is unsubstituted or substituted with:

a) halogen, or

b) phenyl, which is unsubstituted or substituted with 1 – 5 substituents independently selected from halogen, OH,  $\text{C}_{1-6}$ alkyl, and  $\text{OC}_{1-6}$ alkyl, wherein the  $\text{C}_{1-6}$ alkyl is linear or branched and optionally substituted with 1 – 5 halogens,

or wherein  $\text{R}^{1305}$  and  $\text{R}^{1306}$  together with the nitrogen atom to which they are attached form a heterocyclic ring selected from azetidine, pyrrolidine, piperidine, piperazine, and morpholine wherein said heterocyclic ring is unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy,

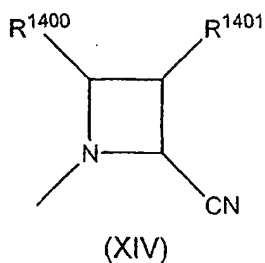


C<sub>1-6</sub>alkyl, and C<sub>1-6</sub>alkoxy, wherein alkyl and alkoxy are unsubstituted with one to five halogens;

- R<sup>1304</sup> and R<sup>1307</sup> are hydrogen;

or wherein the group PM

has the formula XIV:



- wherein R<sup>1400</sup> is H and R<sup>1401</sup> is hydrogen atom (-H); or fluoro, or cyano.

### Synthesis of the compounds of the present invention

The compounds of formula (I) according to the present invention can be obtained by the general method, characterized in that the amino acid amide of the general formula

A-B

is synthesized, wherein

- A is NR<sup>1</sup>R<sup>2</sup> - C(=EWG1)-(CR<sup>3</sup>R<sup>4</sup>)<sub>n</sub> - CR<sup>5</sup>R<sup>6</sup> - CR<sup>7</sup>R<sup>8</sup> - CR<sup>9</sup>(NR<sup>10</sup>R<sup>11</sup>) - C(=EWG2) as defined above, and

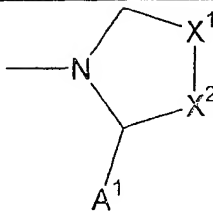
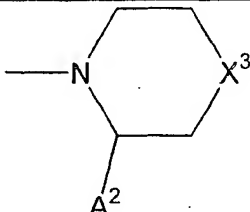
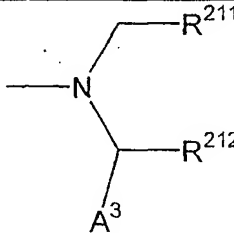
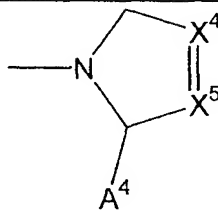
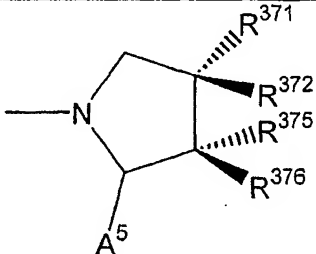
- B is a proline mimetic (PM) as defined above, and

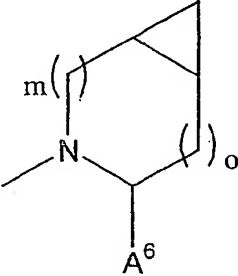
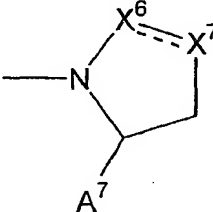
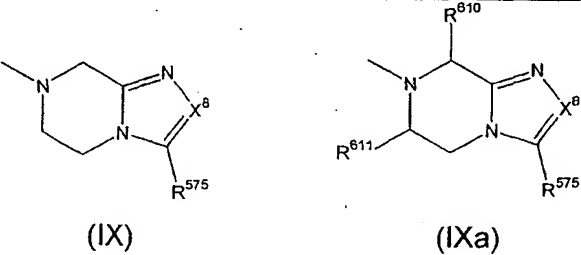
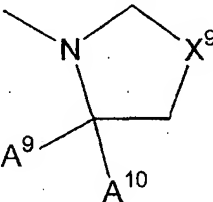
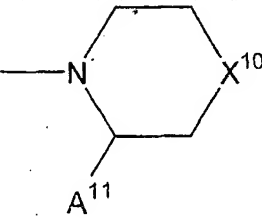
- wherein their production is performed by starting from X-A-Y or X-A(Z)-Y (in case of trifunctional amino acids for A) by substitution with B, wherein A and B are defined as described above, X stands for an  $\alpha$ -amino-protecting group commonly used in peptide chemistry, preferably the t-butyloxycarbonyl residue, Z represents a common side chain-protecting group, preferably of the t-butyl-type (t-butyloxycarbonyl, t-butyl ester, O- or S-t-butyl) depending on the structure of the trifunctional amino acid, and Y means hydroxy, active ester, preferably pentafluorophenyl or N-hydroxysuccinimide ester, according the method common in the peptide chemistry for attachment of the amide bond, desirably via the anhydride mixture technique or the active ester method, then the protecting groups used for X and Z are removed with the deblocking method common in the peptide chemistry for the above-mentioned of the t-butyl type through acidolysis, and if necessary, the products are purified through recrystallization or through column chromatography on Sephadex G10 or weakly acidic ion exchange resin.

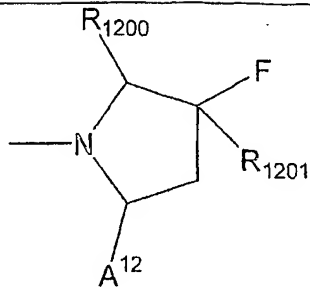
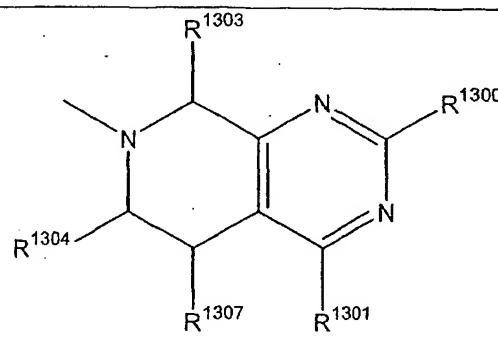
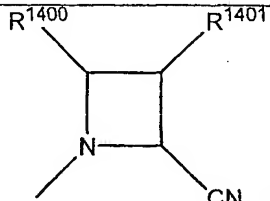
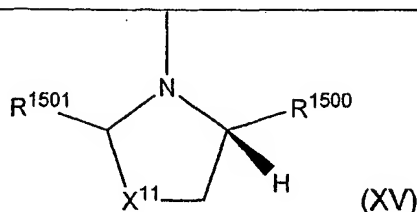
Specific synthetic routes and synthetic schemes for the respective proline mimetics of the present invention are well known in the state of the art. References which disclose these synthetic routes and synthetic schemes of compounds which comprise the proline mimetics of the present invention, are listed in table 2. These references are incorporated herein in their entirety and are part of the present invention with regard to the synthesis of the compounds of the present invention comprising the respective proline mimetics.

Table 2: References disclosing the synthetic routes and synthesis schemes of proline mimetics according to the present invention

Reference for synthetic route and synthesis schemes	Proline mimetic (PM)
--	----------------------

<p>WO 01/34594 A1, pp. 21 – 22, International Publication Date: May 17, 2001</p>	 <p>(II)</p>
<p>WO 01/34594 A1, pp. 48 - 49, International Publication Date: May 17, 2001</p>	 <p>(III)</p>
<p>WO 01/34594 A1, p. 57, International Publication Date: May 17, 2001</p>	 <p>(IV)</p>
<p>WO 01/55105 A1, pp. 17 – 18, International Publication Date: August 2, 2001</p>	 <p>(V)</p>
<p>1. WO 02/38541, especially engl. version EP 1333025A1 thereof, pp. 8 – 14, Date of Publication: August 6, 2003 2. when <math>A^5 = H</math> and <math>R^{371}</math>, <math>R^{375}</math> and <math>R^{376} = F</math> WO 03/101449A2, pp. 6 – 10, International Publication Date: December 11, 2003</p>	 <p>(VI)</p>

<p>WO 01/68603A2, pp. 8 – 11, International. Publication Date: September 20, 2001</p>	 <p>(VII)</p>
<p>WO 02/083128A1, pp. 7 – 10, International. Publication Date: October 24, 2002</p>	 <p>(VIII)</p>
<p>1. for PM (IX): WO 03/004498A1, pp. 24 – 28, International. Publication Date: January 16, 2003 2. for PM (IXa): WO 03/082817A2, pp. 29 – 37, International. Publication Date: October 9, 2003</p>	 <p>(IX) (IXa)</p>
<p>WO 03/000180A2, pp. 26 – 35, International Publication Date: January 3, 2003</p>	 <p>(X)</p>
<p>WO 03/000181A2, pp. 25 – 32, International Publication Date: January 3, 2003</p>	 <p>(XI)</p>

<p>WO 03/00250A1, pp. 11 – 14, International Publication Date: January 3, 2003</p>	 <p>(XII)</p>
<p>WO 04/007468A1, pp. 28 – 39, International Publication Date : January 22, 2004</p>	 <p>(XIII)</p>
<p>WO 04/007446A1, pp. 12 – 16, International Publication Date : January 22, 2004</p>	 <p>(XIV)</p>
<p>WO 04/026822A2, pp. 32 – 40, International Publication Date: April 1, 2004</p>	 <p>(XV)</p>

A further preferred embodiment of the present invention comprises the compound of the general formula (I) according to any one of the embodiments of the present invention

- in combination with acarbose, or
- in combination with metformin; or

- in combination with acarbose and metformin.

In a further preferred embodiment the DP IV inhibitors of the general formula (I) of the present invention, optionally in combination with QC inhibitor, can be used in combination with

- (a) other DP IV inhibitors
- (b) insulin sensitizers selected from the group consisting of
  - (i) PPAR agonists,
  - (ii) biguanides, and
  - (iii) protein tyrosin phosphatase-1B (PTP-1B) inhibitors;
- (c) insulin and insulin mimetics;
- (d) sulfonylureas and other insulin secretagogues;
- (e)  $\alpha$ -glucosidase inhibitors;
- (f) glucagon receptor agonists;
- (g) GLP-1; GLP-1 mimetics, e.g. NN-2211 (liraglutide from Novo Nordisk), and GLP-1 receptor agonists;
- (h) GLP-2; GLP-2 mimetics, e.g. ALX-0600 (teduglutide from NPS Allelix Corp.) and GLP-2 receptor agonists;
- (i) exendin-4 and exendin-4 mimetics, e.g. exenatide (AC-2993, synthetic exendin-4 from Amylin/Eli Lilly);
- (j) GIP, GIP mimetics, and GIP receptor agonists;
- (k) PACAP, PACAP mimetics, and PACAP receptor 3 agonists;
- (l) cholesterol lowering agents selected from the group consisting of
  - (i) HMG-CoA reductase inhibitors,
  - (ii) sequestrants,
  - (iii) nicotiny alcohol, nicotinic acid and salts thereof,
  - (iv) PPAR $\alpha$  agonists,
  - (v) PPAR $\alpha/\gamma$  dual agonists,
  - (vi) inhibitors of cholesterol absorption,
  - (vii) acyl CoA:cholesterol acyltransferase inhibitors, and
  - (viii) antioxidants;
- (m) PPAR $\delta$  agonists;

- (n) antiobesity compounds;
- (o) an ileal bile acid transporter inhibitor; and
- (p) anti-inflammatory agents.

A further preferred embodiment of the present invention comprises the compound of the general formula (I) according to any one of the embodiments of the present invention mentioned above

- in combination with a gene therapeutic expression system for GLP-1 comprising a viral vector comprising
  - (a) a polynucleotide sequence encoding GLP-1 (glucagon like peptide - 1); and
  - (b) a polynucleotide sequence encoding a signal sequence upstream of (a); and
  - (c) a polyadenylation signal downstream of (a); and
  - (d) a polynucleotide sequence encoding a proteolytic cleavage site located between the polynucleotide sequence encoding GLP-1 and the polynucleotide sequence encoding the signal sequence; and
  - (e) wherein the expression of GLP-1 underlies a constitutive promoter or is controlled by a regulatable promoter;
  - (f) wherein, optionally, the viral vector comprises a polynucleotide sequence encoding GIP (glucose dependent insulinotropic peptide);
  - (g) wherein, optionally, the viral vector is encompassed by a mammalian cell.

and / or

- in combination with a gene therapeutic expression system for GIP comprising a viral vector comprising
  - (a) a polynucleotide sequence encoding GIP (glucose dependent insulinotropic peptide); and
  - (b) a polynucleotide sequence encoding a signal sequence upstream of (a); and

- (c) a polyadenylation signal downstream of (a); and
- (d) a polynucleotide sequence encoding a proteolytic cleavage site located between the polynucleotide sequence encoding GIP and the polynucleotide sequence encoding the signal sequence; and
- (e) wherein the expression of GIP underlies a constitutive promoter or is controlled by a regulatable promoter;
- (f) wherein, optionally, the viral vector comprises a polynucleotide sequence encoding GLP-1 (glucagon like peptide 1);
- (g) wherein, optionally, the viral vector is encompassed by a mammalian cell.

A further preferred embodiment of the present invention comprises the compound of the general formula (I) in combination with a gene therapeutic expression system for GLP-1 and / or GIP according to any one of the embodiments of the present invention mentioned above

wherein

- the signal sequence upstream of the gene of interest (GLP-1; GIP) is the murine immunoglobulin  $\kappa$  signal sequence or the glia monster exendin signal sequence; and / or
- the polyadenylation signal downstream of the gene of interest (GLP-1; GIP) is derived from simian virus 40 (SV 40); and /or
- the proteolytic cleavage site is cleaved by furin pretease; and/ or
- the gene delivery vector for expression the gene of interest is an adenoviral, retroviral, leniviral, adeno associated viral vector; and /or
- the constitutive promoter is a cytomegalovirus (CMV) promotor, or a Rous sarcoma long-terminal repeat (LTR) sequence, and the SV 40 early gene gene promoter; and the inducible promoter is the Tet-On<sup>TM</sup> / Tet-Off<sup>TM</sup> system available from Clontech; and /or
- the mammalian cell is a primate or rodent cell, preferably a human cell, more preferably a human hepatocyte.



A further preferred embodiment of the present invention comprises the compound of the general formula (I) in combination with a glutaminy cyclase (QC) inhibitor, and, additionally, a gene therapeutic expression system for GLP-1 and / or GIP according to any one of the embodiments of the present invention mentioned above.

In a preferred embodiment, the compound of the general formula (I) according to the present invention is used in the form of a pharmaceutical composition comprising a composition according to any one the embodiments mentioned, and optionally a pharmaceutical acceptable diluent and/or carrier.

In a preferred embodiment, the compound of the general formula (I) according to the present invention is used in the form of a composition or a pharmaceutical composition according to any one of the preceding embodiments for the preparation of a medicament for the inhibition of dipeptidyl peptidase IV.

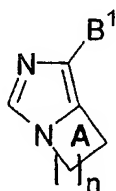
In a preferred embodiment, the compound of the general formula (I) according to the present invention is used in the form of a composition or a pharmaceutical composition according to any one of the preceding embodiments for the preparation of a medicament for the treatment of disorders related to the inhibition of dipeptidyl peptidase IV. Examples for disorders related to the inhibition of DP IV which can be treated by DP IV inhibitors according to the present invention are listed under item "Indications".

In a more preferred embodiment, the compound of the general formula (I) according to the present invention, which is an inhibitor of dipeptidyl peptidase (DPIV), may be used in combination with an inhibitor of glutaminy cyclase (QC).

In a preferred embodiment, the compound of the general formula (I) according to the present invention may be used in the form of a composition or a pharmaceutical composition according to any one of the preceding embodiments for the preparation of a medicament for the treatment of diseases of mammals that can be treated by

modulation of DPIV- and, optionally, QC activity, in a mammal, especially for the treatment of metabolic diseases in humans.

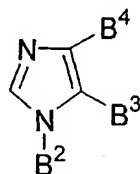
Inhibitors of glutaminy cyclase are, e.g. compounds having the general formula 1, including the pharmaceutically acceptable salts and including all stereoisomers thereof:



formula 1

wherein n is 1, 2, 3 or 4, preferably 2 and 3, most preferred 2, and A can be any saturated or unsaturated heterocycle and wherein B¹ is H or a branched or unbranched alkyl chain, a branched or unbranched alkenyl chain, a branched or unbranched alkynyl chain, carbocyclic, aryl, heteroaryl, heterocyclic, aza-amino acid, amino acid or a mimetic thereof, aza-peptide, peptide or a mimetic thereof; all of the above residues optionally being substituted.

Further inhibitors of glutaminy cyclase are, e.g. compounds which can be described generally by the formula 2, including the pharmaceutically acceptable salts and including all stereoisomers thereof:

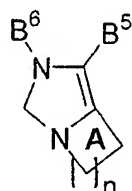


formula 2

wherein B², B³ and B⁴ are independently H or a branched or unbranched alkyl chain, a branched or unbranched alkenyl chain, a branched or unbranched alkynyl chain, carbocyclic, aryl, heteroaryl, heterocyclic, aza-amino acid, amino acid or a mimetic

thereof, aza-peptide, peptide or a mimetic thereof; all of the above residues optionally being substituted.

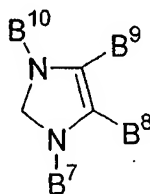
Furthermore, inhibitors of glutaminy cyclase are compounds which can be described generally by the formula 3, including the pharmaceutically acceptable salts and including all stereoisomers thereof:



formula 3

wherein  $n$  is 1, 2, 3 or 4, preferably 2 and 3, most preferred 2, and A can be any saturated or unsaturated heterocycle and wherein  $B^5$  and  $B^6$  are independently H or a branched or unbranched alkyl chain, a branched or unbranched alkenyl chain, a branched or unbranched alkynyl chain, carbocyclic, aryl, heteroaryl, heterocyclic, aza-amino acid, amino acid or a mimetic thereof, aza-peptide, peptide or a mimetic thereof; all of the above residues optionally being substituted.

Furthermore, inhibitors of glutaminy cyclase are compounds which can be described generally by the formula 4 and the pharmaceutically acceptable salts thereof, including all stereoisomers:

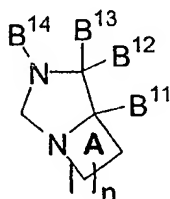


formula 4

wherein  $B^7$ ,  $B^8$ ,  $B^9$  and  $B^{10}$  are independently H or a branched or unbranched alkyl chain, a branched or unbranched alkenyl chain, a branched or unbranched alkynyl chain, carbocyclic, aryl, heteroaryl, heterocyclic, aza-amino acid, amino acid or a

mimetic thereof, aza-peptide, peptide or a mimetic thereof; all of the above residues optionally being substituted.

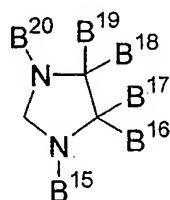
Furthermore, inhibitors of glutaminy cyclase are compounds which can be described generally by the formula 5 and the pharmaceutically acceptable salts thereof, including all stereoisomers:



formula 5

wherein  $n$  is 1, 2, 3 or 4, preferably 2 and 3, especially 2, and A can be any saturated or unsaturated heterocycle and wherein  $B^{11}$ ,  $B^{12}$ ,  $B^{13}$  and  $B^{14}$  are independently H or a branched or unbranched alkyl chain, a branched or unbranched alkenyl chain, a branched or unbranched alkynyl chain, carbocyclic, aryl, heteroaryl, heterocyclic, aza-amino acid, amino acid or a mimetic thereof, aza-peptide, peptide or a mimetic thereof; all of the above residues optionally being substituted.

Furthermore, inhibitors of glutaminy cyclase are compounds which can be described generally by the formula 6 and the pharmaceutically acceptable salts thereof, including all stereoisomers:

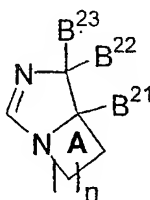


formula 6

wherein  $B^{15}$ ,  $B^{16}$ ,  $B^{17}$ ,  $B^{18}$ ,  $B^{19}$  and  $B^{20}$  are independently H or a branched or unbranched alkyl chain, a branched or unbranched alkenyl chain, a branched or unbranched alkynyl chain, carbocyclic, aryl, heteroaryl, heterocyclic, aza-amino acid,

amino acid or a mimetic thereof, aza-peptide, peptide or a mimetic thereof; all of the above residues optionally being substituted.

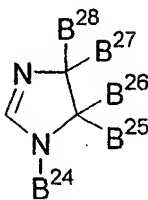
In addition, inhibitors of glutaminyl cyclase are compounds which can be described generally by the formula 7, including the pharmaceutically acceptable salts and including all stereoisomers thereof:



formula 7

wherein  $n$  is 1, 2, 3 or 4, preferably 2 and 3, especially 2, and A can be any saturated or unsaturated heterocycle and wherein  $B^{21}$ ,  $B^{22}$  and  $B^{23}$  are independently H or a branched or unbranched alkyl chain, a branched or unbranched alkenyl chain, a branched or unbranched alkynyl chain, carbocyclic, aryl, heteroaryl, heterocyclic, aza-amino acid, amino acid or a mimetic thereof, peptide or a mimetic thereof; all of the above residues optionally being substituted.

Furthermore, inhibitors of glutaminyl cyclase are compounds which can be described generally by the formula 8, including the pharmaceutically acceptable salts and including all stereoisomers thereof:

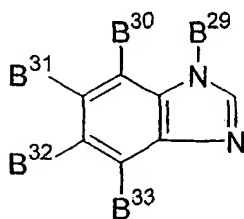


formula 8

wherein  $B^{24}$ ,  $B^{25}$ ,  $B^{26}$ ,  $B^{27}$  and  $B^{28}$  are independently H or a branched or unbranched alkyl chain, a branched or unbranched alkenyl chain, a branched or unbranched alkynyl chain, carbocyclic, aryl, heteroaryl, heterocyclic, aza-amino acid, amino acid

or a mimetic thereof, aza-peptide, peptide or a mimetic thereof; all of the above residues optionally being substituted.

Furthermore, inhibitors of glutaminyl cyclase are compounds which can be described generally by the formula 9 or the pharmaceutically acceptable salts thereof, including all stereoisomers:



formula 9

wherein  $B^{29}$ ,  $B^{30}$ ,  $B^{31}$ ,  $B^{32}$  and  $B^{33}$  are independently H or a branched or unbranched alkyl chain, a branched or unbranched alkenyl chain, a branched or unbranched alkynyl chain, carbocyclic, aryl, heteroaryl, heterocyclic, aza-amino acid, amino acid or a mimetic thereof, aza-peptide, peptide or a mimetic thereof; all of the above residues optionally being substituted.

Examples of inhibitors of glutaminyl cyclase are imidazole and its derivatives and histidine and its derivatives. Structures and  $K_i$ -values for inhibition of glutaminyl cyclase activity are shown in tables 3 and 4. The results are described in detail in example 9.

**Table 3: Inhibitory constants of imidazole derivatives in the human QC catalyzed reaction. Determinations were performed at 30 °C in 0.05 M Tris-HCl pH 8.0, containing 5 mM EDTA.**

Compound	$K_i$ -value (mM)	Structure
<b>core structures</b>		
imidazole	$0.103 \pm 0.004$	

---

benzimidazole	0.138 ±0.005
<b><i>N-1 DERIVATIVES</i></b>	
1-benzylimidazole	0.0071 ±0.0003
1-methylimidazole	0.030 ±0.001
1-vinylimidazole	0.049 ±0.002
oxalic acid diimidazolidide	0.078 ±0.002
N-acetylimidazole	0.107 ±0.003
N-(trimethylsilyl)-imidazole	0.167 ±0.007
N-benzoylimidazole	0.174 ±0.007
1-(2-oxo-2-phenyl-ethyl)- imidazole	0.184 ±0.005
1-(3-aminopropyl)-imidazole	0.41 ±0.01
1-phenylimidazole	no inhibition
1,1'-sulfonyldiimidazole	no inhibition
<b><i>C-4(5) DERIVATIVES</i></b>	
N-omega-acetylhistamine	0.017 ±0.001
L-histidinamide	0.56 ±0.04
H-His-Trp-OH	0.60 ±0.03
L-histidinol	1.53 ±0.12
L-histidine	4.4 ±0.2
4-imidazole-carboxaldehyde	7.6 ±0.7
imidazole-4-carbonic acid methylester	14.5 ±0.6
L-histamine	0.85 ±0.04
<b><i>C-4,5 derivatives</i></b>	
5-hydroxymethyl-4-methyl- imidazole	0.129 ±0.005
4-amino-imidazole-5-carbonic acid amide	15.5 ±0.5

---

---

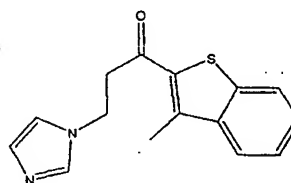
4,5-diphenyl-imidazole	no inhibition
4,5-dicyanoimidazole	no inhibition

**C-2 DERIVATIVES**

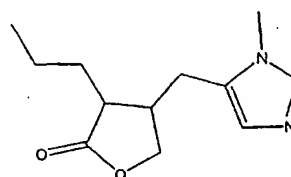
2-methyl-benzylimidazole	0.165 ±0.004
2-ethyl-4-methyl-imidazole	0.58 ±0.04
2-aminobenzimidazole	1.8 ±0.1
2-chloro-1H-benzimidazole	no inhibition

**Others**

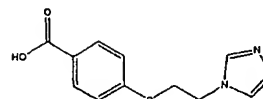
3-(1H-imidazol-1-yl)-1-(3-methylbenzo[b]thiophene-2-yl)propan-1-one	0.0025 ±0.0001
---	----------------



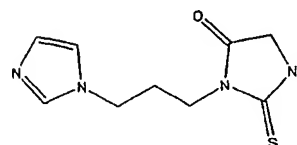
4-[(1-methyl-1H-imidazol-5-yl)methyl]-3-propyldihydrofuran-2-(3H)-one	0.0067 ± 0.0003
---	-----------------



4-[2-(1H-imidazol-1-yl)-ethoxy]benzoic acid	0.0034 ±0.0001
---	----------------



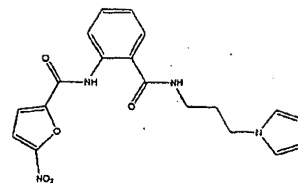
3-[3-(1H-imidazol-1-yl)propyl]-2-thioxoimidazolidin-4-one	0.00041 ±0.00001
---	------------------





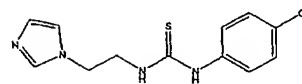
5-nitro-2-[2-([3-(1H-imidazol-1-yl)-propyl]amino)carbonyl]phenyl]furanamide

0.0066  $\pm$  0.0004



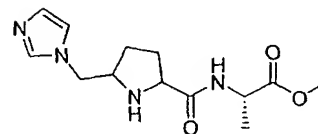
N-(4-chlorophenyl)-N'-[2-(1H-imidazol-1-yl)ethyl]thiourea

0.00165  $\pm$  0.00007



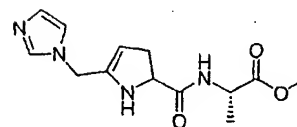
2-[(5-imidazol-1-ylmethyl-pyrrolidine-2-carbonyl)-amino]-propionic acid methyl ester

0,0322  $\pm$  0,0007



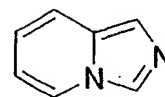
2-[(5-Imidazol-1-ylmethyl-2,3-dihydro-1H-pyrrole-2-carbonyl)-amino]-propionic acid methyl ester

n.d.



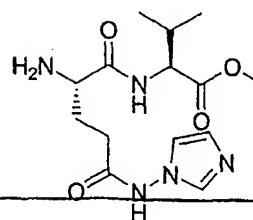
Imidazo[1.5a]pyridine

0.0356  $\pm$  0.0005

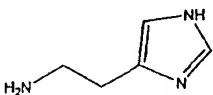
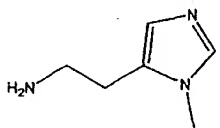
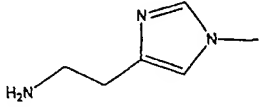


Methyl (2S)-2-[[[(2S)-2-amino-5-(1H-imidazol-1-ylamino)-5-oxopentanoyl]amino]-3-methylbutanoate

0.164  $\pm$  0.004



**Table 4: QC inhibition by L-histamine and its two biological metabolites (also known as *te/e*-methylhistamine).**

Compound	K <sub>i</sub> value (mM)	Structure
L-histamine	0.85 ±0.04	
3-methyl-4-(β-aminoethyl)- imidazole	0.120 ±0.004	
1-methyl-4-(β-aminoethyl)- imidazole	n.i.	

In a more preferred embodiment, the compound of the general formula (I) according to the present invention, optionally in combination with a glutaminyl cyclase inhibitor, is used in the form of a composition or a pharmaceutical composition according to

any one of the preceding embodiments for the preparation of a medicament for the treatment of non-insulin dependent diabetes mellitus (type 2), for the improvement of impaired glucose tolerance (IGT), impaired fasting glucose (IFG) and impaired glucose metabolism (IGM) by lowering elevated blood glucose levels in response to an oral glucose challenge, for the treatment of glucosuria, and disturbances of signal action at the cells of the islets of Langerhans and insulin sensitivity in the peripheral tissue in the postprandial phase of mammals, especially in humans.

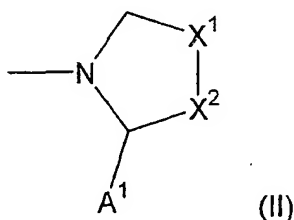
In a further preferred embodiment, the compound of the general formula (I) according to the present invention, optionally in combination with a glutaminyl cyclase inhibitor, is used in the form of a composition or a pharmaceutical composition according to any one of the preceding embodiments for the preparation of a medicament for the treatment of hyperlipidemia, metabolic acidosis, diabetic neuropathy and nephropathy and of sequelae caused by diabetes mellitus in mammals, metabolism-related hypertension and cardiovascular sequelae caused by hypertension in mammals; for the prophylaxis or treatment of skin diseases and diseases of the mucosae, autoimmune diseases and inflammatory conditions, and for the prophylaxis or treatment of psychosomatic, neuropsychiatric and depressive illness, and neurodegenerative diseases such as anxiety, depression, sleep disorders, chronic fatigue, schizophrenia, epilepsy, nutritional disorders, spasm and chronic pain.

In a preferred embodiment, the compounds according to the invention and their corresponding pharmaceutically acceptable acid addition salt forms, are useful in treating conditions mediated by DPPIV or DPPIV-like enzymes, such as arthritis, obesity, immune and autoimmune disorders, allograft transplantation, cancer, neuronal disorders and dermal diseases.

Furthermore, an embodiment of the present invention comprises a simple method for the treatment of those disorders.

**Examples:**

The present invention can be carried out by the following examples, which are illustrating, but not limiting the scope of the invention.

**Examples for prolin mimetics of formula (II):**

(100) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = CR^{51}R^{52}$  and  $R^{51} = H$  and  $R^{52} = H$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -C\equiv N$ , namely glutaminyl-1N-(2-cyano-pyrrolidine).

(101) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = S$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -C\equiv N$ , namely glutaminyl-3N-(4-cyano-thiazolidine).

(102) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = SO$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -C\equiv N$ , namely glutaminyl-3N-(4-cyano-1-oxo-thiazolidine).

(103) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = SO_2$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -C\equiv N$ , namely glutaminyl-3N-(4-cyano-1-dioxo-thiazolidine).

(104) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = SO$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = H$ , namely glutaminyl-3N-(1-oxo-thiazolidine).

(105) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = SO_2$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -H$ , namely glutaminyl-3N-(1-dioxo-thiazolidine).

- (106) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = NR^{53}$  and  $R^{53} = H$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -H$ , namely glutaminy-1N-(-imidazolidine).
- (107) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = NR^{53}$  and  $R^{53} = H$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -C\equiv N$ , namely glutaminy-1N-(5-cyano-imidazolidine).
- (108) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = NR^{53}$  and  $R^{53} = CH_3$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -H$ , namely glutaminy-1N-(3N-methyl-imidazolidine).
- (109) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = NR^{53}$  and  $R^{53} = CH_3$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -C\equiv N$ , namely glutaminy-1N-(3N-methyl-5-cyano-imidazolidine).
- (110) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = NR^{53}$  and  $R^{53} = C_6H_5$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -H$ , namely glutaminy-1N-(3N-phenyl-imidazolidine).
- (111) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = NR^{53}$  and  $R^{53} = C_6H_5$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -C\equiv N$ , namely glutaminy-1N-(3N-phenyl-5-cyano-imidazolidine).
- (112) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = O$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -H$ , namely glutaminy-3N-(oxazolidine).
- (113) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = O$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -C\equiv N$ , namely glutaminy-3N-(4-cyano-oxazolidine).
- (114) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = CR^{51}R^{52}$  and  $R^{51} = H$  and  $R^{52} = CH_3$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -C\equiv N$ , namely glutaminy-N-(2-cyano-4-methyl-pyrrolidine).

(115) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = CR^{51}R^{52}$  and  $R^{51} = CH_3$  and  $R^{52} = CH_3$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -C\equiv N$ , namely glutaminy-N-(2-cyano-4,4-dimethyl-pyrrolidine).

(116) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = CR^{51}R^{52}$  and  $R^{51} = H$  and  $R^{52} = H$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = CH_3$  and  $R^{55} = H$  and  $A^1 = -C\equiv N$ , namely glutaminy-N-(2-cyano-3-methyl-pyrrolidine).

(117) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = CR^{51}R^{52}$  and  $R^{51} = H$  and  $R^{52} = H$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = CH_3$  and  $R^{55} = CH_3$  and  $A^1 = -C\equiv N$ , namely glutaminy-N-(2-cyano-3,3-dimethyl-pyrrolidine).

(118) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = CR^{51}R^{52}$  and  $R^{51} = CH_3$  and  $R^{52} = H$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = CH_3$  and  $A^1 = -C\equiv N$ , namely glutaminy-N-(2-cyano-3,4-dimethyl-pyrrolidine).

(119) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = CR^{51}R^{52}$  and  $R^{51} = CH_3$  and  $R^{52} = H$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -H$ , namely glutaminy-N-(3-methyl-pyrrolidine).

(120) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = CR^{51}R^{52}$  and  $R^{51} = CH_3$  and  $R^{52} = CH_3$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -H$ , namely glutaminy-N-(3,3-dimethyl-pyrrolidine).

(121) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = CR^{51}R^{52}$  and  $R^{51} = CH_3$  and  $R^{52} = H$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = CH_3$  and  $R^{55} = H$  and  $A^1 = -C\equiv N$ , namely glutaminy-N-(3,4-dimethyl-pyrrolidine).

(122) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = CR^{51}R^{52}$  and  $R^{51} = CF_3$  and  $R^{52} = H$  and  $X^2 = CR^{54}R^{55}$

and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -C\equiv N$ , namely glutaminyl-N-(2-cyano-4-trifluormethyl-pyrrolidine).

(123) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = CR^{51}R^{52}$  and  $R^{51} = H$  and  $R^{52} = H$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = CF_3$  and  $R^{55} = H$  and  $A^1 = -C\equiv N$ , namely glutaminyl-N-(2-cyano-3-trifluormethyl-pyrrolidine).

(124) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = CR^{51}R^{52}$  and  $R^{51} = CF_3$  and  $R^{52} = H$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = CF_3$  and  $R^{55} = H$  and  $A^1 = -C\equiv N$ , namely glutaminyl-N-(2-cyano-3,4-bis(trifluormethyl)-pyrrolidine).

(125) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = CR^{51}R^{52}$  and  $R^{51} = CF_3$  and  $R^{52} = H$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = H$ , namely glutaminyl-N-(3-trifluormethyl-pyrrolidine).

(126) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = CR^{51}R^{52}$  and  $R^{51} = CF_3$  and  $R^{52} = H$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = CF_3$  and  $R^{55} = H$  and  $A^1 = -H$ , namely glutaminyl-N-(3,4-bis(trifluormethyl)-pyrrolidine).

(127) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = CR^{51}R^{52}$  and  $R^{51} = H$  and  $R^{52} = H$  and  $X^2 = O$  and  $A^1 = -C\equiv N$ , namely glutaminyl-3N-(2-cyano-oxazolidine).

(128) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = CR^{51}R^{52}$  and  $R^{51} = H$  and  $R^{52} = H$  and  $X^2 = S$  and  $A^1 = -C\equiv N$ , namely glutaminyl-3N-(2-cyano-thiazolidine).

(129) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = CR^{51}R^{52}$  and  $R^{51} = H$  and  $R^{52} = H$  and  $X^2 = SO$  and  $A^1 = -C\equiv N$ , namely glutaminyl-3N-(2-cyano-1-oxo-thiazolidine).

- (130) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = CR^{51}R^{52}$  and  $R^{51} = H$  and  $R^{52} = H$  and  $X^2 = SO_2$  and  $A^1 = -C\equiv N$ , namely glutaminy-3N-(2-cyano-1,1-dioxo-thiazolidine).
- (131) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = CR^{51}R^{52}$  and  $R^{51} = H$  and  $R^{52} = H$  and  $X^2 = NR^{56}$  and  $R^{56} = H$  and  $A^1 = -C\equiv N$ , namely glutaminy-1N-(2-cyano-imidazolidine).
- (132) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = CR^{51}R^{52}$  and  $R^{51} = H$  and  $R^{52} = H$  and  $X^2 = NR^{56}$  and  $R^{56} = CH_3$  and  $A^1 = -C\equiv N$ , namely glutaminy-1N-(2-cyano-3N-methyl-imidazolidine).
- (133) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = CR^{51}R^{52}$  and  $R^{51} = H$  and  $R^{52} = H$  and  $X^2 = NR^{56}$  and  $R^{56} = C_6H_5$  and  $A^1 = -C\equiv N$ , namely glutaminy-1N-(2-cyano-3N-phenyl-imidazolidine).
- (134) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = NR^{53}$  and  $R^{53} = H$  and  $X^2 = NR^{56}$  and  $R^{56} = H$  and  $A^1 = -H$ , namely glutaminy-4N-(1,2,4-triazolidine).
- (135) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = NR^{53}$  and  $R^{53} = H$  and  $X^2 = NR^{56}$  and  $R^{56} = H$  and  $A^1 = -C\equiv N$ , namely glutaminy-4N-(3-cyano-1,2,4-triazolidine).
- (136) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = NR^{53}$  and  $R^{53} = CH_3$  and  $X^2 = NR^{56}$  and  $R^{56} = H$  and  $A^1 = -H$ , namely glutaminy-4N-(1N-methyl-1,2,4-triazolidine).
- (137) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = NR^{53}$  and  $R^{53} = CH_3$  and  $X^2 = NR^{56}$  and  $R^{56} = H$  and  $A^1 = -C\equiv N$ , namely glutaminy-4N-(1N-methyl-3-cyano-1,2,4-triazolidine).
- (138) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = NR^{53}$  and  $R^{53} = H$  and  $X^2 = NR^{56}$  and  $R^{56} = CH_3$  and  $A^1 = -H$ , namely glutaminy-4N-(2N-methyl-1,2,4-triazolidine).



- (139) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = NR^{53}$  and  $R^{53} = H$  and  $X^2 = NR^{56}$  and  $R^{56} = CH_3$  and  $A^1 = -C\equiv N$ , namely glutaminy-4N-(2N-methyl-3-cyano-1,2,4-triazolidine).
- (140) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = NR^{53}$  and  $R^{53} = CH_3$  and  $X^2 = NR^{56}$  and  $R^{56} = CH_3$  and  $A^1 = -C\equiv N$ , namely glutaminy-4N-(1N,2N-dimethyl-3-cyano-1,2,4-triazolidine).
- (141) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = CR^{51}R^{52}$  and  $R^{51} = H$  and  $R^{52} = H$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -CHO$ , namely glutaminy-1N-(pyrrolidine-2-carbaldehyde).
- (142) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = S$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -CHO$ , namely glutaminy-3N-(thiazolidine-4-carbaldehyde).
- (143) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = O$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -CHO$ , namely glutaminy-3N-(oxazolidine-4-carbaldehyde).
- (144) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = NR^{53}$  and  $R^{53} = H$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -CHO$ , namely glutaminy-1N-(imidazolidine-5-carbaldehyde).
- (145) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = NR^{53}$  and  $R^{53} = CH_3$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -CHO$ , namely glutaminy-1N-(3N-methyl-imidazolidine-5-carbaldehyde).
- (146) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = CR^{51}R^{52}$  and  $R^{51} = H$  and  $R^{52} = H$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -SO_3H$ , namely glutaminy-1N-(pyrrolidine-2-sulphonic acid).

- (147) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = S$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -SO_3H$ , namely glutaminy-3N-(thiazolidine-4-sulphonic acid).
- (148) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = O$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -SO_3H$ , namely glutaminy-3N-(oxazolidine-4-sulphonic acid).
- (149) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = NR^{53}$  and  $R^{53} = H$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -SO_3H$ , namely glutaminy-1N-(imidazolidine-5-sulphonic acid).
- (150) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = CR^{51}R^{52}$  and  $R^{51} = H$  and  $R^{52} = H$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -SO_2NH_2$ , namely glutaminy-1N-(pyrrolidine-2-sulphonamide).
- (151) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = S$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -SO_2NH_2$ , namely glutaminy-3N-(thiazolidine-4-sulphonamide).
- (152) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = O$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -SO_2NH_2$ , namely glutaminy-3N-(oxazolidine-4-sulphonamide).
- (153) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = NR^{53}$  and  $R^{53} = H$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -SO_2NH_2$ , namely glutaminy-1N-(imidazolidine-5-sulphonamide).
- (154) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = S$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -CO-NH_2$ , namely glutaminy-3N-(thiazolidine-4-carboxamide).
- (155) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = O$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -CO-NH_2$ , namely glutaminy-3N-(oxazolidine-4-carboxamide).

- (156) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = NR^{53}$  and  $R^{53} = H$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -CO-NH_2$ , namely glutaminyl-1N-(imidazolidine-5-carboxamide).
- (157) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = S$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -COOH$ , namely glutaminyl-3N-(thiazolidine-4-carboxylic acid).
- (158) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = O$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -COOH$ , namely glutaminyl-3N-(oxazolidine-4-carboxylic acid).
- (159) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = NR^{53}$  and  $R^{53} = H$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -COOH$ , namely glutaminyl-1N-(imidazolidine-5-carboxylic acid).
- (160) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = CR^{51}R^{52}$  and  $R^{51} = H$  and  $R^{52} = H$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -OP(=O)(OH)_2$ , namely glutaminyl-1N-(pyrrolidine-2-phosphoric acid).
- (161) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = S$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -OP(=O)(OH)_2$ , namely glutaminyl-3N-(thiazolidine-4-phosphoric acid).
- (162) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = O$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -OP(=O)(OH)_2$ , namely glutaminyl-3N-(oxazolidine-4-phosphoric acid).
- (163) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = NR^{53}$  and  $R^{53} = H$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -OP(=O)(OH)_2$ , namely glutaminyl-1N-(imidazolidine-5-phosphoric acid).
- (164) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = CR^{51}R^{52}$  and  $R^{51} = H$  and  $R^{52} = H$  and  $X^2 = CR^{54}R^{55}$

and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -P(=O)(OH)_2$ , namely glutaminy-1N-(pyrrolidine-2-phosphonic acid).

(165) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = S$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -P(=O)(OH)_2$ , namely glutaminy-3N-(thiazolidine-4-phosphonic acid).

(166) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = O$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -P(=O)(OH)_2$ , namely glutaminy-3N-(oxazolidine-4-phosphonic acid).

(167) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = NR^{53}$  and  $R^{53} = H$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -P(=O)(OH)_2$ , namely glutaminy-1N-(imidazolidine-5-phosphonic acid).

(168) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = CR^{51}R^{52}$  and  $R^{51} = H$  and  $R^{52} = H$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -P(=O)(OR^{76})(OR^{77})$  and  $R^{76} = -C_6H_5$ , and  $R^{77} = -C_6H_5$ , namely glutaminy-(pyrrolidine-2-phosphonic acid diphenyl ester).

(169) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = S$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -P(=O)(OR^{76})(OR^{77})$  and  $R^{76} = -C_6H_5$ , and  $R^{77} = -C_6H_5$ , namely glutaminy-3N-(thiazolidine-4-phosphonic acid diphenyl ester).

(170) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = O$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -P(=O)(OR^{76})(OR^{77})$  and  $R^{76} = -C_6H_5$ , and  $R^{77} = -C_6H_5$ , namely glutaminy-3N-(oxazolidine-4-phosphonic acid diphenyl ester).

(171) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = NR^{53}$  and  $R^{53} = H$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -P(=O)(OR^{76})(OR^{77})$  and  $R^{76} = -C_6H_5$ , and  $R^{77} = -C_6H_5$ , namely glutaminy-1N-(imidazolidine-5-phosphonic acid diphenyl ester).

- (172) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = CR^{51}R^{52}$  and  $R^{51} = H$  and  $R^{52} = H$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = 2H\text{-tetrazol-5-yl}$ , namely glutaminy-1N-(2-(2H-tetrazol-5-yl)-pyrrolidine).
- (173) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = S$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = 2H\text{-tetrazol-5-yl}$ , namely glutaminy-3N-(4-(2H-tetrazol-5-yl)-thiazolidine).
- (174) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = O$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = 2H\text{-tetrazol-5-yl}$ , namely glutaminy-3N-(4-(2H-tetrazol-5-yl)-oxazolidine).
- (175) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = NR^{53}$  and  $R^{53} = H$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = 2H\text{-tetrazol-5-yl}$ , namely glutaminy-1N-(5-(2H-tetrazol-5-yl)-imidazolidine).
- (176) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = CR^{51}R^{52}$  and  $R^{51} = H$  and  $R^{52} = H$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -B(OH)_2$ , namely glutaminy-1N-(2-(boronic acid)-pyrrolidine).
- (177) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = S$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -B(OH)_2$ , namely glutaminy-3N-(4-(boronic acid)-thiazolidine).
- (178) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = O$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -B(OH)_2$ , namely glutaminy-3N-(4-(boronic acid)-oxazolidine).
- (179) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = NR^{53}$  and  $R^{53} = H$  and  $X^2 = CR^{54}R^{55}$  and  $R^{54} = H$  and  $R^{55} = H$  and  $A^1 = -B(OH)_2$ , namely glutaminy-1N-(5-(boronic acid)-imidazolidine).

(180) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = CR^{51}R^{52}$  and  $R^{51} = H$  and  $R^{52} = H$  and  $X^2 = S$  and  $A^1 = -COOH$ , namely glutaminyl-3N-(thiazolidine-2-carboxylic acid).

(181) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = CR^{51}R^{52}$  and  $R^{51} = H$  and  $R^{52} = H$  and  $X^2 = O$  and  $A^1 = -COOH$ , namely glutaminyl-3N-(oxazolidine-2-carboxylic acid).

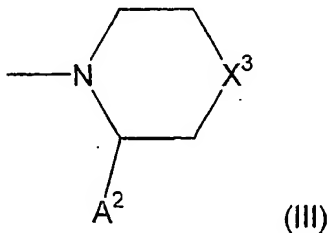
(182) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = CR^{51}R^{52}$  and  $R^{51} = H$  and  $R^{52} = H$  and  $X^2 = NR^{56}$  and  $R^{56} = H$  and  $A^1 = -COOH$ , namely glutaminyl-1N-(imidazolidine-2-carboxylic acid).

(183) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = CR^{51}R^{52}$  and  $R^{51} = H$  and  $R^{52} = H$  and  $X^2 = S$  and  $A^1 = 2H\text{-tetrazol-5-yl}$ , namely glutaminyl-3N-(2-(2H-tetrazol-5-yl)-thiazolidine).

(184) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = CR^{51}R^{52}$  and  $R^{51} = H$  and  $R^{52} = H$  and  $X^2 = O$  and  $A^1 = 2H\text{-tetrazol-5-yl}$ , namely glutaminyl-3N-(2-(2H-tetrazol-5-yl)-oxazolidine).

(185) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^1 = CR^{51}R^{52}$  and  $R^{51} = H$  and  $R^{52} = H$  and  $X^2 = NR^{56}$  and  $R^{56} = H$  and  $A^1 = 2H\text{-tetrazol-5-yl}$ , namely glutaminyl-1N-(2-(2H-tetrazol-5-yl)-imidazolidine).

**Examples for prolin mimetics of formula (III):**



- (300) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = CR^{131}R^{132}$  and  $R^{131} = H$  and  $R^{132} = H$  and  $A^2 = -H$ , namely glutaminy-1N-(piperidine).
- (301) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = O$  and  $A^2 = -H$ , namely glutaminy-4N-(morpholine).
- (302) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = S$  and  $A^2 = -H$ , namely glutaminy-4N-(thiomorpholine).
- (303) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = SO$  and  $A^2 = -H$ , namely glutaminy-4N-(1-oxo-thiomorpholine).
- (304) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = SO_2$  and  $A^2 = -H$ , namely glutaminy-4N-(1,1-dioxo-thiomorpholine).
- (305) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = NR^{133}$  and  $R^{133} = H$  and  $A^2 = -H$ , namely glutaminy-1N-(piperazine).
- (306) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = NR^{133}$  and  $R^{133} = CH_3$  and  $A^2 = -H$ , namely glutaminy-1N-(4-methyl-piperazine).
- (307) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = NR^{133}$  and  $R^{133} = C_6H_5$  and  $A^2 = -H$ , namely glutaminy-1N-(4-phenyl-piperazine).
- (308) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = CR^{131}R^{132}$  and  $R^{131} = CH_3$  and  $R^{132} = H$  and  $A^2 = -H$ , namely glutaminy-1N-(4-methyl-piperidine).
- (309) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = CR^{131}R^{132}$  and  $R^{131} = CF_3$  and  $R^{132} = H$  and  $A^2 = -H$ , namely glutaminy-1N-(4-trifluormethyl-piperidine).

(310) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = CR^{131}R^{132}$  and  $R^{131} = C_6H_5$  and  $R^{132} = H$  and  $A^2 = -H$ , namely glutaminy-1N-(4-phenyl-piperidine).

(311) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = CR^{131}R^{132}$  and  $R^{131} = NH_2$  and  $R^{132} = H$  and  $A^2 = -H$ , namely glutaminy-1N-(4-amino-piperidine).

(312) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = CR^{131}R^{132}$  and  $R^{131} = H$  and  $R^{132} = H$  and  $A^2 = -C\equiv N$ , namely glutaminy-1N-(2-cyano-piperidine).

(313) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = O$  and  $A^2 = -C\equiv N$ , namely glutaminy-4N-(3-cyano-morpholine).

(314) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = S$  and  $A^2 = -C\equiv N$ , namely glutaminy-4N-(3-cyano-4-thiomorpholine).

(315) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = NR^{133}$  and  $R^{133} = H$  and  $A^2 = -C\equiv N$ , namely glutaminy-1N-(2-cyano-piperazine).

(316) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = NR^{133}$  and  $R^{133} = CH_3$  and  $A^2 = -C\equiv N$ , namely glutaminy-1N-(2-cyano-4-methyl-piperazine).

(317) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = NR^{133}$  and  $R^{133} = C_6H_5$  and  $A^2 = -C\equiv N$ , namely glutaminy-1N-(2-cyano-4-phenyl-piperazine).

(318) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = CR^{131}R^{132}$  and  $R^{131} = CH_3$  and  $R^{132} = H$  and  $A^2 = -C\equiv N$ , namely glutaminy-1N-(2-cyano-4-methyl-piperidine).



- (319) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = CR^{131}R^{132}$  and  $R^{131} = CF_3$  and  $R^{132} = H$  and  $A^2 = -C\equiv N$ , namely glutaminy-1N-(2-cyano-4-trifluormethyl-piperidine).
- (320) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = CR^{131}R^{132}$  and  $R^{131} = C_6H_5$  and  $R^{132} = H$  and  $A^2 = -C\equiv N$ , namely glutaminy-1N-(2-cyano-4-phenyl-piperidine).
- (321) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = CR^{131}R^{132}$  and  $R^{131} = NH_2$  and  $R^{132} = H$  and  $A^2 = -C\equiv N$ , namely glutaminy-1N-(2-cyano-4-amino-piperidine).
- (322) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = CR^{131}R^{132}$  and  $R^{131} = H$  and  $R^{132} = H$  and  $A^2 = -COOH$ , namely glutaminy-1N-(piperidine-2-carboxylic acid).
- (323) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = O$  and  $A^2 = -COOH$ , namely glutaminy-4N-(morpholine-3-carboxylic acid).
- (324) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = S$  and  $A^2 = -COOH$ , namely glutaminy-4N-(thiomorpholine-3-carboxylic acid).
- (325) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = NR^{133}$  and  $R^{133} = H$  and  $A^2 = -COOH$ , namely glutaminy-1N-(piperazine-2-carboxylic acid).
- (326) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = NR^{133}$  and  $R^{133} = CH_3$  and  $A^2 = -COOH$ , namely glutaminy-1N-(4-methyl-piperazine-2-carboxylic acid).
- (327) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = NR^{133}$  and  $R^{133} = C_6H_5$  and  $A^2 = -COOH$ , namely glutaminy-1N-(4-phenyl-piperazine-2-carboxylic acid).

- (328) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = CR^{131}R^{132}$  and  $R^{131} = CH_3$  and  $R^{132} = H$  and  $A^2 = -COOH$ , namely glutaminy-1N-(4-methyl-piperidine-2-carboxylic acid).
- (329) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = CR^{131}R^{132}$  and  $R^{131} = CF_3$  and  $R^{132} = H$  and  $A^2 = -COOH$ , namely glutaminy-1N-(4-trifluormethyl-piperidine-2-carboxylic acid).
- (330) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = CR^{131}R^{132}$  and  $R^{131} = C_6H_5$  and  $R^{132} = H$  and  $A^2 = -COOH$ , namely glutaminy-1N-(4-phenyl-piperidine-2-carboxylic acid).
- (331) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = CR^{131}R^{132}$  and  $R^{131} = NH_2$  and  $R^{132} = H$  and  $A^2 = -COOH$ , namely glutaminy-1N-(4-amino-piperidine-2-carboxylic acid).
- (332) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = CR^{131}R^{132}$  and  $R^{131} = H$  and  $R^{132} = H$  and  $A^2 = -B(OH)_2$ , namely glutaminy-1N-(piperidine-2-boronic acid).
- (333) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = O$  and  $A^2 = -B(OH)_2$ , namely glutaminy-4N-(morpholine-3-boronic acid).
- (334) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = S$  and  $A^2 = -B(OH)_2$ , namely glutaminy-4N-(thiomorpholine-3-boronic acid).
- (335) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = NR^{133}$  and  $R^{133} = H$  and  $A^2 = -B(OH)_2$ , namely glutaminy-1N-(piperazine-2-boronic acid).
- (336) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = NR^{133}$  and  $R^{133} = CH_3$  and  $A^2 = -B(OH)_2$ , namely glutaminy-1N-(4-methyl-piperazine-2-boronic acid).

(337) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = NR^{133}$  and  $R^{133} = C_6H_5$  and  $A^2 = -B(OH)_2$ , namely glutaminy-1N-(4-phenyl-piperazine-2-boronic acid).

(338) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = CR^{131}R^{132}$  and  $R^{131} = CH_3$  and  $R^{132} = H$  and  $A^2 = -B(OH)_2$ , namely glutaminy-1N-(4-methyl-piperidine-2-boronic acid).

(339) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = CR^{131}R^{132}$  and  $R^{131} = CF_3$  and  $R^{132} = H$  and  $A^2 = -B(OH)_2$ , namely glutaminy-1N-(4-trifluormethyl-piperidine-2-boronic acid).

(340) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = CR^{131}R^{132}$  and  $R^{131} = C_6H_5$  and  $R^{132} = H$  and  $A^2 = -B(OH)_2$ , namely glutaminy-1N-(4-phenyl-piperidine-2-boronic acid).

(341) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = CR^{131}R^{132}$  and  $R^{131} = NH_2$  and  $R^{132} = H$  and  $A^2 = -B(OH)_2$ , namely glutaminy-1N-(4-amino-piperidine-2-boronic acid).

(342) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = CR^{131}R^{132}$  and  $R^{131} = H$  and  $R^{132} = H$  and  $A^2 = -P(=O)(OR^{196})(OR^{197})$  and  $R^{196} = -C_6H_5$ , and  $R^{197} = -C_6H_5$ , namely glutaminy-1N-(piperidine-2-phosphonic acid diphenyl ester).

(343) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = O$  and  $A^2 = -P(=O)(OR^{196})(OR^{197})$  and  $R^{196} = -C_6H_5$ , and  $R^{197} = -C_6H_5$ , namely glutaminy-4N-(morpholine-3-phosphonic acid diphenyl ester).

(344) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = S$  and  $A^2 = -P(=O)(OR^{196})(OR^{197})$  and  $R^{196} = -C_6H_5$ , and  $R^{197} = -C_6H_5$ , namely glutaminy-4N-(thiomorpholine-3-phosphonic acid diphenyl ester).

(345) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = NR^{133}$  and  $R^{133} = H$  and  $A^2 = -P(=O)(OR^{196})(OR^{197})$  and

$R^{196} = -C_6H_5$ , and  $R^{197} = -C_6H_5$ , namely glutaminy-1N-(piperazine-2-phosphonic acid diphenyl ester).

(346) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = NR^{133}$  and  $R^{133} = CH_3$  and  $A^2 = -P(=O)(OR^{196})(OR^{197})$  and  $R^{196} = -C_6H_5$ , and  $R^{197} = -C_6H_5$ , namely glutaminy-1N-(4-methyl-piperazine-2-phosphonic acid diphenyl ester).

(347) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = CR^{131}R^{132}$  and  $R^{131} = NH_2$  and  $R^{132} = H$  and  $A^2 = -P(=O)(OR^{196})(OR^{197})$  and  $R^{196} = -C_6H_5$ , and  $R^{197} = -C_6H_5$ , namely glutaminy-1N-(4-amino-piperidine-2-phosphonic acid diphenyl ester).

(348) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = CR^{131}R^{132}$  and  $R^{131} = H$  and  $R^{132} = H$  and  $A^2 = 2H$ -tetrazol-5-yl, namely glutaminy-1N-(2-(2H-tetrazol-5-yl)-piperidine)

(349) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = O$  and  $A^2 = 2H$ -tetrazol-5-yl, namely glutaminy-4N-(3-(2H-tetrazol-5-yl)-morpholine).

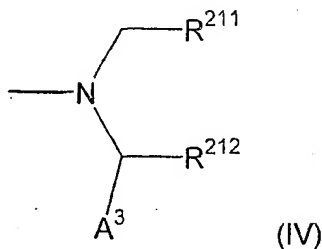
(350) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = S$  and  $A^2 = 2H$ -tetrazol-5-yl, namely glutaminy-4N-(3-(2H-tetrazol-5-yl)-thiomorpholine).

(351) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = NR^{133}$  and  $R^{133} = H$  and  $A^2 = 2H$ -tetrazol-5-yl, namely glutaminy-1N-(2-(2H-tetrazol-5-yl)-piperazine).

(352) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = NR^{133}$  and  $R^{133} = CH_3$  and  $A^2 = 2H$ -tetrazol-5-yl, namely glutaminy-1N-(2-(2H-tetrazol-5-yl)-4-methyl-piperazine).

(353) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^3 = CR^{131}R^{132}$  and  $R^{131} = NH_2$  and  $R^{132} = H$  and  $A^2 = 2H$ -tetrazol-5-yl, namely glutaminy-1N-(2-(2H-tetrazol-5-yl)-4-amino-piperidine).

Examples for prolin mimetics of formula (IV):



(400) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = H$  and  $R^{212} = H$  and  $A^3 = -H$ , namely glutaminy-(N,N-dimethylamid).

(401) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -CH_3$  and  $R^{212} = H$  and  $A^3 = -H$ , namely glutaminy-(N-ethyl-N-methylamid).

(402) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -C_2H_5$  and  $R^{212} = H$  and  $A^3 = -H$ , namely glutaminy-(N-propyl-N-methylamid).

(403) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -C_6H_5$  and  $R^{212} = H$  and  $A^3 = -H$ , namely glutaminy-(N-benzyl-N-methylamid).

(404) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -CH_2C_6H_5$  and  $R^{212} = H$  and  $A^3 = -H$ , namely glutaminy-(N-phenethyl-N-methylamid).

(405) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -CH_3$  and  $R^{212} = CH_3$  and  $A^3 = -H$ , namely glutaminy-(N,N-diethylamid).

- (406) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -C_2H_5$  and  $R^{212} = CH_3$  and  $A^3 = -H$ , namely glutaminy-(N-propyl-N-ethylamid).
- (407) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -C_6H_5$  and  $R^{212} = CH_3$  and  $A^3 = -H$ , namely glutaminy-(N-benzyl-N-ethylamid).
- (408) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -CH_2C_6H_5$  and  $R^{212} = CH_3$  and  $A^3 = -H$ , namely glutaminy-(N-phenethyl-N-ethylamid).
- (409) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -C_2H_5$  and  $R^{212} = -C_2H_5$  and  $A^3 = -H$ , namely glutaminy-(N,N-dipropylamid).
- (410) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -C_6H_5$  and  $R^{212} = -C_2H_5$  and  $A^3 = -H$ , namely glutaminy-(N-benzyl-N-propylamid).
- (411) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -CH_2C_6H_5$  and  $R^{212} = -C_2H_5$  and  $A^3 = -H$ , namely glutaminy-(N-phenethyl-N-propylamid).
- (412) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -C_6H_5$  and  $R^{212} = -C_6H_5$  and  $A^3 = -H$ , namely glutaminy-(N,N-dibenzylamid).
- (413) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -CH_2C_6H_5$  and  $R^{212} = -C_6H_5$  and  $A^3 = -H$ , namely glutaminy-(N-phenethyl-N-benzylamid).
- (414) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -CH_2C_6H_5$  and  $R^{212} = -CH_2C_6H_5$  and  $A^3 = -H$ , namely glutaminy-(N,N-di(phenethyl)amid).

- (415) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = H$  and  $R^{212} = H$  and  $A^3 = 2H$ -tetrazol-5-yl, namely glutaminy-(N-methyl-N-((2H-tetrazol-5-yl)methyl)amid).
- (416) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -CH_3$  and  $R^{212} = H$  and  $A^3 = 2H$ -tetrazol-5-yl, namely glutaminy-(N-ethyl-N-((2H-tetrazol-5-yl)methyl)amid).
- (417) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -C_2H_5$  and  $R^{212} = H$  and  $A^3 = 2H$ -tetrazol-5-yl, namely glutaminy-(N-propyl-N-((2H-tetrazol-5-yl)methyl)amid).
- (418) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -C_6H_5$  and  $R^{212} = H$  and  $A^3 = 2H$ -tetrazol-5-yl, namely glutaminy-(N-benzyl-N-((2H-tetrazol-5-yl)methyl)amid).
- (419) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -CH_2C_6H_5$  and  $R^{212} = H$  and  $A^3 = 2H$ -tetrazol-5-yl, namely glutaminy-(N-phenethyl-N-((2H-tetrazol-5-yl)methyl)amid).
- (420) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = H$  and  $R^{212} = -CH_3$  and  $A^3 = 2H$ -tetrazol-5-yl, namely glutaminy-(N-methyl-N-(1-(2H-tetrazol-5-yl)eth-1-yl)amid).
- (421) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = H$  and  $R^{212} = -C_2H_5$  and  $A^3 = 2H$ -tetrazol-5-yl, namely glutaminy-(N-methyl-N-(1-(2H-tetrazol-5-yl)propyl)amid).
- (422) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = H$  and  $R^{212} = -C_6H_5$  and  $A^3 = 2H$ -tetrazol-5-yl, namely glutaminy-(N-methyl-N-( $\alpha$ -(2H-tetrazol-5-yl)benzyl)amid).
- (422) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = H$  and  $R^{212} = -CH_2C_6H_5$  and  $A^3 = 2H$ -tetrazol-5-yl, namely glutaminy-(N-methyl-N-(1-(2H-tetrazol-5-yl)-2-phenyl-eth1-yl)amid).

(423) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -CH_3$  and  $R^{212} = CH_3$  and  $A^3 = 2H\text{-tetrazol-5-yl}$ , namely glutaminy-(N-ethyl-N-(1-(2H-tetrazol-5-yl)eth-1-yl)amid).

(424) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -C_2H_5$  and  $R^{212} = CH_3$  and  $A^3 = 2H\text{-tetrazol-5-yl}$ , namely glutaminy-(N-propyl-N-(1-(2H-tetrazol-5-yl)eth-1-yl)amid).

(425) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -C_6H_5$  and  $R^{212} = CH_3$  and  $A^3 = 2H\text{-tetrazol-5-yl}$ , namely glutaminy-(N-benzyl-N-(1-(2H-tetrazol-5-yl)eth-1-yl)amid).

(426) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -CH_2C_6H_5$  and  $R^{212} = CH_3$  and  $A^3 = 2H\text{-tetrazol-5-yl}$ , namely glutaminy-(N-phenethyl-N-(1-(2H-tetrazol-5-yl)eth-1-yl)amid).

(427) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -CH_3$  and  $R^{212} = -C_2H_5$  and  $A^3 = 2H\text{-tetrazol-5-yl}$ , namely glutaminy-(N-ethyl-N-(1-(2H-tetrazol-5-yl)prop-1-yl)amid).

(428) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -CH_3$  and  $R^{212} = -C_6H_5$  and  $A^3 = 2H\text{-tetrazol-5-yl}$ , namely glutaminy-(N-ethyl-N-( $\alpha$ -(2H-tetrazol-5-yl)benzyl)amid).

(429) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -CH_3$  and  $R^{212} = -CH_2C_6H_5$  and  $A^3 = 2H\text{-tetrazol-5-yl}$ , namely glutaminy-(N-ethyl-N-(1-(2H-tetrazol-5-yl)-2-phenyl-eth-1-yl)amid).

(430) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -C_2H_5$  and  $R^{212} = -C_2H_5$  and  $A^3 = 2H\text{-tetrazol-5-yl}$ , namely glutaminy-(N-propyl-N-(1-(2H-tetrazol-5-yl)prop-1-yl)amid).

(431) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -C_6H_5$  and  $R^{212} = -C_2H_5$  and  $A^3 = 2H\text{-tetrazol-5-yl}$ , namely glutaminy-(N-benzyl-N-(1-(2H-tetrazol-5-yl)prop-1-yl)amid).



- (432) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -CH_2C_6H_5$  and  $R^{212} = -C_2H_5$  and  $A^3 = 2H$ -tetrazol-5-yl, namely glutaminy-(N-phenethyl-N-(1-(2H-tetrazol-5-yl)prop-1-yl)amid).
- (433) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -C_2H_5$  and  $R^{212} = -C_6H_5$  and  $A^3 = 2H$ -tetrazol-5-yl, namely glutaminy-(N-propyl-N-( $\alpha$ -(2H-tetrazol-5-yl)benzyl)amid).
- (434) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -C_2H_5$  and  $R^{212} = -CH_2C_6H_5$  and  $A^3 = 2H$ -tetrazol-5-yl, namely glutaminy-(N-propyl-N-(1-(2H-tetrazol-5-yl)-2-phenyl-eth-1-yl)amid).
- (435) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -C_6H_5$  and  $R^{212} = -C_6H_5$  and  $A^3 = 2H$ -tetrazol-5-yl, namely glutaminy-(N-benzyl-N-( $\alpha$ -(2H-tetrazol-5-yl)benzyl)amid).
- (436) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -CH_2C_6H_5$  and  $R^{212} = -C_6H_5$  and  $A^3 = 2H$ -tetrazol-5-yl, namely glutaminy-(N-phenethyl-N-( $\alpha$ -(2H-tetrazol-5-yl)benzyl)amid).
- (437) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -C_6H_5$  and  $R^{212} = -CH_2C_6H_5$  and  $A^3 = 2H$ -tetrazol-5-yl, namely glutaminy-(N-benzyl-N-(1-(2H-tetrazol-5-yl)-2-phenyl-eth-1-yl)amid).
- (438) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -CH_2C_6H_5$  and  $R^{212} = -CH_2C_6H_5$  and  $A^3 = 2H$ -tetrazol-5-yl, namely glutaminy-(N-phenethyl-N-(1-(2H-tetrazol-5-yl)-2-phenyl-eth-1-yl)amid).
- (439) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = H$  and  $R^{212} = H$  and  $A^3 = -C\equiv N$ , namely glutaminy-(N-methyl-N-(cyanomethyl)amid).
- (440) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -CH_3$  and  $R^{212} = H$  and  $A^3 = -C\equiv N$ , namely glutaminy-(N-ethyl-N-(cyanomethyl)amid).

- (441) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -C_2H_5$  and  $R^{212} = H$  and  $A^3 = -C\equiv N$ , namely glutaminy-(N-propyl-N-(cyanomethyl)amid).
- (442) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -C_6H_5$  and  $R^{212} = H$  and  $A^3 = -C\equiv N$ , namely glutaminy-(N-benzyl-N-(cyanomethyl)amid).
- (443) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -CH_2C_6H_5$  and  $R^{212} = H$  and  $A^3 = -C\equiv N$ , namely glutaminy-(N-phenethyl-N-(cyanomethyl)amid).
- (444) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = H$  and  $R^{212} = -CH_3$  and  $A^3 = -C\equiv N$ , namely glutaminy-(N-methyl-N-(1-cyano-eth-1-yl)amid).
- (445) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = H$  and  $R^{212} = -C_2H_5$  and  $A^3 = -C\equiv N$ , namely glutaminy-(N-methyl-N-(1-cyano-propyl)amid).
- (446) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = H$  and  $R^{212} = -C_6H_5$  and  $A^3 = -C\equiv N$ , namely glutaminy-(N-methyl-N-( $\alpha$ -cyano-benzyl)amid).
- (447) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = H$  and  $R^{212} = -CH_2C_6H_5$  and  $A^3 = -C\equiv N$ , namely glutaminy-(N-methyl-N-(1-cyano-2-phenyl-eth1-yl)amid).
- (448) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -CH_3$  and  $R^{212} = CH_3$  and  $A^3 = -C\equiv N$ , namely glutaminy-(N-ethyl-N-(1-cyano-eth-1-yl)amid).
- (449) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -C_2H_5$  and  $R^{212} = CH_3$  and  $A^3 = -C\equiv N$ , namely glutaminy-(N-propyl-N-(1-cyano-eth-1-yl)amid).

(450) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -C_6H_5$  and  $R^{212} = CH_3$  and  $A^3 = -C\equiv N$ , namely glutaminy-(N-benzyl-N-(1-cyano-eth-1-yl)amid).

(451) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -CH_2C_6H_5$  and  $R^{212} = CH_3$  and  $A^3 = -C\equiv N$ , namely glutaminy-(N-phenethyl-N-(1-cyano-eth-1-yl)amid).

(452) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -CH_3$  and  $R^{212} = -C_2H_5$  and  $A^3 = -C\equiv N$ , namely glutaminy-(N-ethyl-N-(1-cyano-prop-1-yl)amid).

(453) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -CH_3$  and  $R^{212} = -C_6H_5$  and  $A^3 = -C\equiv N$ , namely glutaminy-(N-ethyl-N-( $\alpha$ -cyano-benzyl)amid).

(454) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -CH_3$  and  $R^{212} = -CH_2C_6H_5$  and  $A^3 = -C\equiv N$ , namely glutaminy-(N-ethyl-N-(1-cyano-2-phenyl-eth-1-yl)amid).

(455) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -C_2H_5$  and  $R^{212} = -C_2H_5$  and  $A^3 = -C\equiv N$ , namely glutaminy-(N-propyl-N-(1-cyano-prop-1-yl)amid).

(456) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -C_6H_5$  and  $R^{212} = -C_2H_5$  and  $A^3 = -C\equiv N$ , namely glutaminy-(N-benzyl-N-(1-cyano-prop-1-yl)amid).

(457) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -CH_2C_6H_5$  and  $R^{212} = -C_2H_5$  and  $A^3 = -C\equiv N$ , namely glutaminy-(N-phenethyl-N-(1-cyano-prop-1-yl)amid).

(458) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -C_2H_5$  and  $R^{212} = -C_6H_5$  and  $A^3 = -C\equiv N$ , namely glutaminy-(N-propyl-N-( $\alpha$ -cyano-benzyl)amid).

(459) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -C_2H_5$  and  $R^{212} = -CH_2C_6H_5$  and  $A^3 = -C\equiv N$ , namely glutaminy-(N-propyl-N-(1-cyano-2-phenyl-eth-1-yl)amid).

(460) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -C_6H_5$  and  $R^{212} = -C_6H_5$  and  $A^3 = -C\equiv N$ , namely glutaminy-(N-benzyl-N-( $\alpha$ -cyano-benzyl)amid).

(461) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -CH_2C_6H_5$  and  $R^{212} = -C_6H_5$  and  $A^3 = -C\equiv N$ , namely glutaminy-(N-phenethyl-N-( $\alpha$ -cyano-benzyl)amid).

(462) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -C_6H_5$  and  $R^{212} = -CH_2C_6H_5$  and  $A^3 = -C\equiv N$ , namely glutaminy-(N-benzyl-N-(1-cyano-2-phenyl-eth-1-yl)amid).

(463) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -CH_2C_6H_5$  and  $R^{212} = -CH_2C_6H_5$  and  $A^3 = -C\equiv N$ , namely glutaminy-(N-phenethyl-N-(1-cyano-2-phenyl-eth-1-yl)amid).

(464) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = CF_3$  and  $R^{212} = H$  and  $A^3 = -H$ , namely glutaminy-(N-(2,2,2-trifluorethyl)-N-methylamid).

(465) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = CF_3$  and  $R^{212} = CF_3$  and  $A^3 = -H$ , namely glutaminy-(N,N-bis(2,2,2-trifluorethyl)amid).

(466) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -CH=CH_2$  and  $R^{212} = H$  and  $A^3 = -H$ , namely glutaminy-(N-allyl-N-methylamid).

(467) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -CH=CH_2$  and  $R^{212} = CF_3$  and  $A^3 = -H$ , namely glutaminy-(N-allyl-N-(2,2,2-trifluorethyl)-amid).

(468) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = H$  and  $R^{212} = -CH_3$  and  $A^3 = -\text{tetrazol-5-yl}$ , namely glutaminyl-(N-(1-(tetrazol-5-yl)-eth-1-yl)-N-methylamid).

(469) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -C_2H_5$  and  $R^{212} = H$  and  $A^3 = -\text{tetrazol-5-yl}$ , namely glutaminyl-(N-(1-(tetrazol-5-yl)-methyl-N-propylamid).

(470) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -C_2H_5$  and  $R^{212} = H$  and  $A^3 = -COOH$ , namely glutaminyl-(N-(carboxymethyl)-N-propylamid).

(471) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -C_6H_5$  and  $R^{212} = H$  and  $A^3 = -COOH$ , namely glutaminyl-(N-(carboxymethyl)-N-benzylamid).

(472) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -C_6H_5$  and  $R^{212} = -CH_2C_6H_5$  and  $A^3 = -COOH$ , namely glutaminyl-(N-(1-carboxy-2-phenyl-eth-1-yl)-N-benzylamid).

(473) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -C_6H_5$  and  $R^{212} = -H$  and  $A^3 = -P(=O)(OR^{29})(OR^{30})$  and  $R^{29} = -C_6H_5$  and  $R^{30} = -C_6H_5$  namely glutaminyl-(N-(methyl(O,O-diphenyl phosphonic acid ester))-N-benzylamid).

(474) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -H$  and  $R^{212} = -H$  and  $A^3 = -P(=O)(OR^{29})(OR^{30})$  and  $R^{29} = -C_6H_5$  and  $R^{30} = -C_6H_5$  namely glutaminyl-(N-(methyl(O,O-diphenyl phosphonic acid ester))-N-methylamid).

(475) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -H$  and  $R^{212} = -H$  and  $A^3 = -C\equiv N$  namely glutaminyl-(N-(cyanomethyl)-N-methylamid).

(476) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -CH_3$  and  $R^{212} = -H$  and  $A^3 = -C\equiv N$  namely glutaminyl-(N-(cyanomethyl)-N-ethylamid).

- (477) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -CF_3$  and  $R^{212} = -H$  and  $A^3 = -C\equiv N$  namely glutaminy-(N-(cyanomethyl)-N-(2,2,2-trifluoroethyl)amid).
- (478) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -C_6H_5$  and  $R^{212} = -H$  and  $A^3 = -C\equiv N$  namely glutaminy-(N-(cyanomethyl)-N-benzylamid).
- (479) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -C_6F_5$  and  $R^{212} = -H$  and  $A^3 = -C\equiv N$  namely glutaminy-(N-(cyanomethyl)-N-(pentafluorophenylmethyl)amid).
- (480) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -H$  and  $R^{212} = -CH_3$  and  $A^3 = -C\equiv N$  namely glutaminy-(N-(1-cyano-eth-1-yl)-N-methylamid).
- (481) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -CH_3$  and  $R^{212} = -CH_3$  and  $A^3 = -C\equiv N$  namely glutaminy-(N-(1-cyano-eth-1-yl)-N-ethylamid).
- (482) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -C_6H_5$  and  $R^{212} = -CH_3$  and  $A^3 = -C\equiv N$  namely glutaminy-(N-(1-cyano-eth-1-yl)-N-benzylamid).
- (483) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -H$  and  $R^{212} = -C_6H_5$  and  $A^3 = -C\equiv N$  namely glutaminy-(N-( $\alpha$ -cyano-benzyl)-N-methylamid).
- (484) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -H$  and  $R^{212} = -CF_3$  and  $A^3 = -C\equiv N$  namely glutaminy-(N-(1-cyano-2,2,2-trifluoroeth-1-yl)-N-methylamid).
- (485) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -H$  and  $R^{212} = -H$  and  $A^3 = -B(OH)_2$ , namely glutaminy-(N-(methyl boronic acid)-N-methylamid).

(486) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -CH_3$  and  $R^{212} = -H$  and  $A^3 = -B(OH)_2$ , namely glutaminy-(N-(methyl boronic acid)-N-ethylamid).

(487) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -CF_3$  and  $R^{212} = -H$  and  $A^3 = -B(OH)_2$ , namely glutaminy-(N-(methyl boronic acid)-N-(2,2,2-trifluoroethyl)-amid).

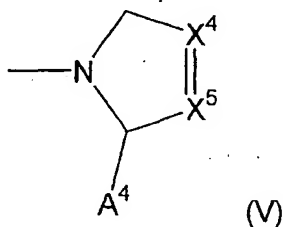
(488) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -C_6H_5$  and  $R^{212} = -H$  and  $A^3 = -B(OH)_2$ , namely glutaminy-(N-(methyl boronic acid)-N-benzylamid).

(489) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -C_6F_5$  and  $R^{212} = -H$  and  $A^3 = -B(OH)_2$ , namely glutaminy-(N-(methyl boronic acid)-N-(pentafluorophenylmethyl)amid).

(490) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -H$  and  $R^{212} = -CH_3$  and  $A^3 = -B(OH)_2$ , namely glutaminy-(N-(1-boronic acid-eth-1-yl)-N-methylamid).

(491) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{211} = -H$  and  $R^{212} = -C_6H_5$  and  $A^3 = -B(OH)_2$ , namely glutaminy-(N-( $\alpha$ -boronic acid)-benzyl)-N-methylamid).

**Examples for prolin mimetics of formula (V):**



(500) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = -H$  and  $X^5 = CR^{292}$  and  $R^{292} = -H$  and  $A^4 = -H$ , namely glutaminy-(2,5-dihydro-1H-pyrrole).

(501) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = -H$  and  $X^5 = CR^{292}$  and  $R^{292} = -H$  and  $A^4 = -COOH$ , namely glutaminy-(2,5-dihydro-1H-pyrrole-2-carboxylic acid).

(502) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = -H$  and  $X^5 = CR^{292}$  and  $R^{292} = -H$  and  $A^4 = -CONH_2$ , namely glutaminy-(2,5-dihydro-1H-pyrrole-2-carboxamide).

(503) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = -H$  and  $X^5 = CR^{292}$  and  $R^{292} = -H$  and  $A^4 = -B(OH)_2$ , namely glutaminy-(2,5-dihydro-1H-pyrrole-2-boronic acid).

(504) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = -H$  and  $X^5 = CR^{292}$  and  $R^{292} = -H$  and  $A^4 = -SO_3H$ , namely glutaminy-(2,5-dihydro-1H-pyrrole-2-sulphonic acid).

(505) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = -H$  and  $X^5 = CR^{292}$  and  $R^{292} = -H$  and  $A^4 = -CF_3$ , namely glutaminy-(2,5-dihydro-2-trifluoromethyl-1H-pyrrole).

(506) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = -H$  and  $X^5 = CR^{292}$  and  $R^{292} = -H$  and  $A^4 = -OP(=O)(OH)_2$ , namely glutaminy-(2,5-dihydro-1H-pyrrole-2-phosphoric acid).

(507) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = -H$  and  $X^5 = CR^{292}$  and  $R^{292} = -H$  and  $A^4 = -P(=O)(OH)_2$ , namely glutaminy-(2,5-dihydro-1H-pyrrole-2-phosphonic acid).

(508) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = -H$  and  $X^5 = CR^{292}$  and  $R^{292} = -H$  and  $A^4 = -OP(=O)(OR^{314})(OR^{315})$  and  $R^{314} = -C_6H_5$  and  $R^{315} = -C_6H_5$ , namely glutaminy-(2,5-dihydro-1H-pyrrole-2-phosphoric acid diphenyl ester).



- (509) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = -H$  and  $X^5 = CR^{292}$  and  $R^{292} = -H$  and  $A^4 = -P(=O)(OR^{316})(OR^{317})$  and  $R^{316} = -C_6H_5$  and  $R^{317} = -C_6H_5$ , namely glutaminyl-(2,5-dihydro-1H-pyrrole-2-phosphonic acid diphenyl ester).
- (510) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = CH_3$  and  $X^5 = CR^{292}$  and  $R^{292} = -H$  and  $A^4 = -C\equiv N$ , namely glutaminyl-(4-methyl-2,5-dihydro-1H-pyrrole-2-carbonitrile).
- (511) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = -C_6H_5$  and  $X^5 = CR^{292}$  and  $R^{292} = -H$  and  $A^4 = -C\equiv N$ , namely glutaminyl-(4-phenyl-2,5-dihydro-1H-pyrrole-2-carbonitrile).
- (512) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = CF_3$  and  $X^5 = CR^{292}$  and  $R^{292} = -H$  and  $A^4 = -C\equiv N$ , namely glutaminyl-(4-trifluoromethyl-2,5-dihydro-1H-pyrrole-2-carbonitrile).
- (513) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = -H$  and  $X^5 = CR^{292}$  and  $R^{292} = CH_3$  and  $A^4 = -C\equiv N$ , namely glutaminyl-(3-methyl-2,5-dihydro-1H-pyrrole-2-carbonitrile).
- (514) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = -H$  and  $X^5 = CR^{292}$  and  $R^{292} = -C_6H_5$  and  $A^4 = -C\equiv N$ , namely glutaminyl-(3-phenyl-2,5-dihydro-1H-pyrrole-2-carbonitrile).
- (515) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = -H$  and  $X^5 = CR^{292}$  and  $R^{292} = CF_3$  and  $A^4 = -C\equiv N$ , namely glutaminyl-(3-trifluoromethyl-2,5-dihydro-1H-pyrrole-2-carbonitrile).
- (516) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = CH_3$  and  $X^5 = CR^{292}$  and  $R^{292} = CH_3$  and  $A^4 = -C\equiv N$ , namely glutaminyl-(3,4-dimethyl-2,5-dihydro-1H-pyrrole-2-carbonitrile).

- (517) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = CH_3$  and  $X^5 = CR^{292}$  and  $R^{292} = -H$  and  $A^4 = -COOH$ , namely glutaminy-(4-methyl-2,5-dihydro-1H-pyrrole-2-carboxylic acid).
- (518) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = -C_6H_5$  and  $X^5 = CR^{292}$  and  $R^{292} = -H$  and  $A^4 = -COOH$ , namely glutaminy-(4-phenyl-2,5-dihydro-1H-pyrrole-2-carboxylic acid).
- (519) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = CF_3$  and  $X^5 = CR^{292}$  and  $R^{292} = -H$  and  $A^4 = -COOH$ , namely glutaminy-(4-trifluoromethyl-2,5-dihydro-1H-pyrrole-2-carboxylic acid).
- (520) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = -H$  and  $X^5 = CR^{292}$  and  $R^{292} = CH_3$  and  $A^4 = -COOH$ , namely glutaminy-(3-methyl-2,5-dihydro-1H-pyrrole-2-carboxylic acid).
- (521) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = -H$  and  $X^5 = CR^{292}$  and  $R^{292} = -C_6H_5$  and  $A^4 = -COOH$ , namely glutaminy-(3-phenyl-2,5-dihydro-1H-pyrrole-2-carboxylic acid).
- (522) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = -H$  and  $X^5 = CR^{292}$  and  $R^{292} = CF_3$  and  $A^4 = -COOH$ , namely glutaminy-(3-trifluoromethyl-2,5-dihydro-1H-pyrrole-2-carboxylic acid).
- (523) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = CH_3$  and  $X^5 = CR^{292}$  and  $R^{292} = CH_3$  and  $A^4 = -COOH$ , namely glutaminy-(3,4-dimethyl-2,5-dihydro-1H-pyrrole-2-carboxylic acid).
- (524) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = CH_3$  and  $X^5 = CR^{292}$  and  $R^{292} = -H$

and  $A^4 = -B(OH)_2$ , namely glutaminy-(4-methyl-2,5-dihydro-1H-pyrrole-2-boronic acid).

(525) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = -C_6H_5$  and  $X^5 = CR^{292}$  and  $R^{292} = -H$  and  $A^4 = -B(OH)_2$ , namely glutaminy-(4-phenyl-2,5-dihydro-1H-pyrrole-2-boronic acid).

(526) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = CF_3$  and  $X^5 = CR^{292}$  and  $R^{292} = -H$  and  $A^4 = -B(OH)_2$ , namely glutaminy-(4-trifluoromethyl-2,5-dihydro-1H-pyrrole-2-boronic acid).

(527) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = -H$  and  $X^5 = CR^{292}$  and  $R^{292} = CH_3$  and  $A^4 = -B(OH)_2$ , namely glutaminy-(3-methyl-2,5-dihydro-1H-pyrrole-2-boronic acid).

(528) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = -H$  and  $X^5 = CR^{292}$  and  $R^{292} = -C_6H_5$  and  $A^4 = -B(OH)_2$ , namely glutaminy-(3-phenyl-2,5-dihydro-1H-pyrrole-2-boronic acid).

(529) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = -H$  and  $X^5 = CR^{292}$  and  $R^{292} = CF_3$  and  $A^4 = -B(OH)_2$ , namely glutaminy-(3-trifluoromethyl-2,5-dihydro-1H-pyrrole-2-boronic acid).

(530) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = CH_3$  and  $X^5 = CR^{292}$  and  $R^{292} = CH_3$  and  $A^4 = -B(OH)_2$ , namely glutaminy-(3,4-dimethyl-2,5-dihydro-1H-pyrrole-2-boronic acid).

(531) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = CH_3$  and  $X^5 = CR^{292}$  and  $R^{292} = -H$  and  $A^4 = -P(=O)(OR^{316})(OR^{317})$  and  $R^{316} = -C_6H_5$  and  $R^{317} = -C_6H_5$ , namely glutaminy-(4-methyl-2,5-dihydro-1H-pyrrole-2-phosphonic acid diphenyl ester).

(532) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = -C_6H_5$  and  $X^5 = CR^{292}$  and  $R^{292} = -H$  and  $A^4 = -P(=O)(OR^{316})(OR^{317})$  and  $R^{316} = -C_6H_5$  and  $R^{317} = -C_6H_5$ , namely glutaminy-(4-phenyl-2,5-dihydro-1H-pyrrole-2-phosphonic acid diphenyl ester).

(533) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = CF_3$  and  $X^5 = CR^{292}$  and  $R^{292} = -H$  and  $A^4 = -P(=O)(OR^{316})(OR^{317})$  and  $R^{316} = -C_6H_5$  and  $R^{317} = -C_6H_5$ , namely glutaminy-(4-trifluoromethyl-2,5-dihydro-1H-pyrrole-2-phosphonic acid diphenyl ester).

(534) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = -H$  and  $X^5 = CR^{292}$  and  $R^{292} = CH_3$  and  $A^4 = -P(=O)(OR^{316})(OR^{317})$  and  $R^{316} = -C_6H_5$  and  $R^{317} = -C_6H_5$ , namely glutaminy-(3-methyl-2,5-dihydro-1H-pyrrole-2-phosphonic acid diphenyl ester).

(535) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = -H$  and  $X^5 = CR^{292}$  and  $R^{292} = -C_6H_5$  and  $A^4 = -P(=O)(OR^{316})(OR^{317})$  and  $R^{316} = -C_6H_5$  and  $R^{317} = -C_6H_5$ , namely glutaminy-(3-phenyl-2,5-dihydro-1H-pyrrole-2-phosphonic acid diphenyl ester).

(536) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = -H$  and  $X^5 = CR^{292}$  and  $R^{292} = CF_3$  and  $A^4 = -P(=O)(OR^{316})(OR^{317})$  and  $R^{316} = -C_6H_5$  and  $R^{317} = -C_6H_5$ , namely glutaminy-(3-trifluoromethyl-2,5-dihydro-1H-pyrrole-2-phosphonic acid diphenyl ester).

(537) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = CH_3$  and  $X^5 = CR^{292}$  and  $R^{292} = CH_3$  and  $A^4 = -P(=O)(OR^{316})(OR^{317})$  and  $R^{316} = -C_6H_5$  and  $R^{317} = -C_6H_5$ , namely glutaminy-(3,4-dimethyl-2,5-dihydro-1H-pyrrole-2-phosphonic acid diphenyl ester).

(538) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = N$  and  $X^5 = CR^{292}$  and  $R^{292} = -H$  and  $A^4 = -H$ , namely glutaminy-(1N-2,5-dihydro-1H-imidazole).

- (539) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = N$  and  $X^5 = CR^{292}$  and  $R^{292} = -H$  and  $A^4 = -C\equiv N$ , namely glutaminy-(1N-2,5-dihydro-1H-imidazole-5-carbonitrile).
- (540) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = N$  and  $X^5 = CR^{292}$  and  $R^{292} = -H$  and  $A^4 = -COOH$ , namely glutaminy-(1N-2,5-dihydro-1H-imidazole-5-carboxylic acid).
- (541) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = N$  and  $X^5 = CR^{292}$  and  $R^{292} = -H$  and  $A^4 = -CONH_2$ , namely glutaminy-(1N-2,5-dihydro-1H-imidazole-5-carboxamide).
- (542) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = N$  and  $X^5 = CR^{292}$  and  $R^{292} = -H$  and  $A^4 = -B(OH)_2$ , namely glutaminy-(1N-2,5-dihydro-1H-imidazole-5-boronic acid).
- (543) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = N$  and  $X^5 = CR^{292}$  and  $R^{292} = -H$  and  $A^4 = -SO_3H$ , namely glutaminy-(1N-2,5-dihydro-1H-imidazole-5-sulfonic acid).
- (544) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = N$  and  $X^5 = CR^{292}$  and  $R^{292} = -H$  and  $A^4 = -P(=O)(OR^{316})(OR^{317})$  and  $R^{316} = -C_6H_5$  and  $R^{317} = -C_6H_5$ , namely glutaminy-(1N-2,5-dihydro-1H-imidazole-5-phosphonic acid diphenyl ester).
- (545) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = -H$  and  $X^5 = N$  and  $A^4 = -C\equiv N$ , namely glutaminy-(1N-2,5-dihydro-1H-imidazole-2-carbonitrile).
- (546) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = -H$  and  $X^5 = N$  and  $A^4 = -COOH$ , namely glutaminy-(1N-2,5-dihydro-1H-imidazole-2-carboxylic acid).
- (547) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = -H$  and  $X^5 = N$  and  $A^4 = -CONH_2$ , namely glutaminy-(1N-2,5-dihydro-1H-imidazole-2-carboxamide).

(548) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = -H$  and  $X^5 = N$  and  $A^4 = -B(OH)_2$ , namely glutaminy-(1N-2,5-dihydro-1H-imidazole-2-boronic acid).

(549) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = -H$  and  $X^5 = N$  and  $A^4 = -SO_3H$ , namely glutaminy-(1N-2,5-dihydro-1H-imidazole-2-sulfonic acid).

(550) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = -H$  and  $X^5 = N$  and  $A^4 = -P(=O)(OR^{316})(OR^{317})$  and  $R^{316} = -C_6H_5$  and  $R^{317} = -C_6H_5$ , namely glutaminy-(1N-2,5-dihydro-1H-imidazole-2-phosphonic acid diphenyl ester).

(551) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = -CF_3$  and  $X^5 = N$  and  $A^4 = -H$ , namely glutaminy-(4-trifluoromethyl-2,5-dihydro-1H-imidazole).

(552) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = -CF_3$  and  $X^5 = N$  and  $A^4 = -C\equiv N$ , namely glutaminy-(4-trifluoromethyl-2,5-dihydro-1H-imidazole-2-carbonitrile).

(553) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = -CF_3$  and  $X^5 = N$  and  $A^4 = -B(OH)_2$ , namely glutaminy-(4-trifluoromethyl-2,5-dihydro-1H-imidazole-2-boronic acid).

(554) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = CR^{291}$  and  $R^{291} = -CF_3$  and  $X^5 = N$  and  $A^4 = -P(=O)(OR^{316})(OR^{317})$  and  $R^{316} = -C_6H_5$  and  $R^{317} = -C_6H_5$ , namely glutaminy-(4-trifluoromethyl-2,5-dihydro-1H-imidazole-2-phosphonic acid diphenyl ester).

(555) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = N$  and  $X^5 = CR^{292}$  and  $R^{292} = -CF_3$  and  $A^4 = -C\equiv N$ , namely glutaminy-(4-trifluoromethyl-2,5-dihydro-1H-imidazole-5-carbonitrile).

(556) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = N$  and  $X^5 = CR^{292}$  and  $R^{292} = -CF_3$  and  $A^4 = -B(OH)_2$ , namely glutaminy-(4-trifluoromethyl-2,5-dihydro-1H-imidazole-5-boronic acid).

(557) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = N$  and  $X^5 = CR^{292}$  and  $R^{292} = -CF_3$  and  $A^4 = -P(=O)(OR^{316})(OR^{317})$  and  $R^{316} = -C_6H_5$  and  $R^{317} = -C_6H_5$ , namely glutaminyl-(4-trifluoromethyl-2,5-dihydro-1H-imidazole-5-phosphonic acid diphenyl ester).

(558) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = N$  and  $X^5 = N$  and  $A^4 = -H$ , namely glutaminyl-(4N-3,5-dihydro-4H-1,2,4-triazole).

(559) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = N$  and  $X^5 = N$  and  $A^4 = -C\equiv N$ , namely glutaminyl-(4N-3,5-dihydro-4H-1,2,4-triazole-3-carbonitrile).

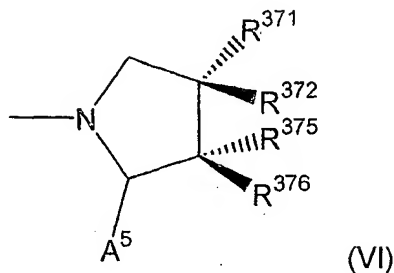
(560) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = N$  and  $X^5 = N$  and  $A^4 = -COOH$ , namely glutaminyl-(4N-3,5-dihydro-4H-1,2,4-triazole-3-carboxylic acid).

(561) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = N$  and  $X^5 = N$  and  $A^4 = -CO-NH_2$ , namely glutaminyl-(4N-3,5-dihydro-4H-1,2,4-triazole-3-carboxamide).

(562) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = N$  and  $X^5 = N$  and  $A^4 = -B(OH)_2$ , namely glutaminyl-(4N-3,5-dihydro-4H-1,2,4-triazole-3-boronic acid).

(563) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = N$  and  $X^5 = N$  and  $A^4 = -P(=O)(OH)_2$ , namely glutaminyl-(4N-3,5-dihydro-4H-1,2,4-triazole-3-phosphonic acid).

(564) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^4 = N$  and  $X^5 = N$  and  $A^4 = -P(=O)(OR^{316})(OR^{317})$  and  $R^{316} = -C_6H_5$  and  $R^{317} = -C_6H_5$ , namely glutaminyl-(4N-3,5-dihydro-4H-1,2,4-triazole-3-phosphonic acid diphenyl ester).

**Examples for prolin mimetics of formula (VI):**

(600) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine,, wherein  $R^{371} = F$  and  $R^{372} = H$  and  $R^{375} = H$  and  $R^{376} = H$  and  $A^5 = -H$ , namely glutaminy-(3R-fluoro-pyrrolidine).

(601) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = H$  and  $R^{372} = F$  and  $R^{375} = H$  and  $R^{376} = H$  and  $A^5 = -H$ , namely glutaminy-(3S-fluoro-pyrrolidine).

(602) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = F$  and  $R^{372} = F$  and  $R^{375} = H$  and  $R^{376} = H$  and  $A^5 = -H$ , namely glutaminy-(3,3-difluoro-pyrrolidine).

(603) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = F$  and  $R^{372} = H$  and  $R^{375} = F$  and  $R^{376} = H$  and  $A^5 = -H$ , namely glutaminy-(meso-3,4-difluoro-pyrrolidine).

(604) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = F$  and  $R^{372} = H$  and  $R^{375} = H$  and  $R^{376} = F$  and  $A^5 = -H$ , namely glutaminy-(3S,4S-difluoro-pyrrolidine).

(605) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = H$  and  $R^{372} = F$  and  $R^{375} = F$  and  $R^{376} = H$  and  $A^5 = -H$ , namely glutaminy-(3R,4R-difluoro-pyrrolidine).



- (606) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = -OH$  and  $R^{372} = H$  and  $R^{375} = H$  and  $R^{376} = H$  and  $A^5 = -H$ , namely glutaminy-(3R-hydroxy-pyrrolidine).
- (607) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = H$  and  $R^{372} = -OH$  and  $R^{375} = H$  and  $R^{376} = H$  and  $A^5 = -H$ , namely glutaminy-(3S-hydroxy-pyrrolidine).
- (608) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} + R^{372} = (=O)$  and  $R^{375} = H$  and  $R^{376} = H$  and  $A^5 = -H$ , namely glutaminy-(3-oxo-pyrrolidine).
- (609) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = F$  and  $R^{372} = H$  and  $R^{375} = H$  and  $R^{376} = H$  and  $A^5 = -C\equiv N$ , namely glutaminy-(4R-fluoro-pyrrolidine-2S-carbonitrile).
- (610) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = H$  and  $R^{372} = F$  and  $R^{375} = H$  and  $R^{376} = H$  and  $A^5 = -C\equiv N$ , namely glutaminy-(4S-fluoro-pyrrolidine-2S-carbonitrile).
- (611) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = F$  and  $R^{372} = F$  and  $R^{375} = H$  and  $R^{376} = H$  and  $A^5 = -C\equiv N$ , namely glutaminy-(4,4-difluoro-pyrrolidine-2-carbonitrile).
- (612) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = H$  and  $R^{372} = H$  and  $R^{375} = F$  and  $R^{376} = H$  and  $A^5 = -C\equiv N$ , namely glutaminy-(3S-fluoro-pyrrolidine-2S-carbonitrile).
- (613) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = F$  and  $R^{372} = H$  and  $R^{375} = F$  and  $R^{376} = H$  and  $A^5 = -C\equiv N$ , namely glutaminy-(3S,4R-difluoro-pyrrolidine-2S-carbonitrile).
- (614) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = H$  and  $R^{372} = F$  and  $R^{375} = F$  and  $R^{376} = H$  and  $A^5 = -C\equiv N$ , namely glutaminy-(3S,4S-difluoro-pyrrolidine-2S-carbonitrile).

- (615) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = H$  and  $R^{372} = H$  and  $R^{375} = H$  and  $R^{376} = F$  and  $A^5 = -C\equiv N$ , namely glutaminy-(3R-fluoro-pyrrolidine-2S-carbonitrile) (Epimer zu 197).
- (616) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = H$  and  $R^{372} = F$  and  $R^{375} = H$  and  $R^{376} = F$  and  $A^5 = -C\equiv N$ , namely glutaminy-(3R,4R-fluoro-pyrrolidine-2S-carbonitrile) (Epimer zu 197).
- (617) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = F$  and  $R^{372} = H$  and  $R^{375} = H$  and  $R^{376} = F$  and  $A^5 = -C\equiv N$ , namely glutaminy-(3R,4S-fluoro-pyrrolidine-2S-carbonitrile) (Epimer zu 197).
- (618) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = -H$  and  $R^{372} = -H$  and  $R^{375} = -F$  and  $R^{376} = -F$  and  $A^5 = -C\equiv N$ , namely glutaminy-(3,3-difluoro-pyrrolidine-2S-carbonitrile).
- (619) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = -F$  and  $R^{372} = -F$  and  $R^{375} = -F$  and  $R^{376} = -F$  and  $A^5 = -C\equiv N$ , namely glutaminy-(3,3,4,4,-tetrafluoro-pyrrolidine-2S-carbonitrile).
- (620) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = F$  and  $R^{372} = H$  and  $R^{375} = H$  and  $R^{376} = H$  and  $A^5 = -COOH$ , namely glutaminy-(4R-fluoro-pyrrolidine-2S-carboxylic acid).
- (621) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = H$  and  $R^{372} = F$  and  $R^{375} = H$  and  $R^{376} = H$  and  $A^5 = -COOH$ , namely glutaminy-(4S-fluoro-pyrrolidine-2S-carboxylic acid).
- (622) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = F$  and  $R^{372} = F$  and  $R^{375} = H$  and  $R^{376} = H$  and  $A^5 = -COOH$ , namely glutaminy-(4,4-difluoro-pyrrolidine-2-carboxylic acid).
- (623) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = H$  and  $R^{372} = H$  and  $R^{375} = F$  and  $R^{376} = H$  and  $A^5 = -COOH$ , namely glutaminy-(3S-fluoro-pyrrolidine-2S-carboxylic acid).

- (624) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = F$  and  $R^{372} = H$  and  $R^{375} = F$  and  $R^{376} = H$  and  $A^5 = -COOH$ , namely glutaminy-(3S,4R-difluoro-pyrrolidine-2S-carboxylic acid).
- (625) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = H$  and  $R^{372} = F$  and  $R^{375} = F$  and  $R^{376} = H$  and  $A^5 = -COOH$ , namely glutaminy-(3S,4S-difluoro-pyrrolidine-2S-carboxylic acid).
- (626) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = H$  and  $R^{372} = H$  and  $R^{375} = H$  and  $R^{376} = F$  and  $A^5 = -COOH$ , namely glutaminy-(3R-fluoro-pyrrolidine-2S-carboxylic acid).
- (627) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = H$  and  $R^{372} = F$  and  $R^{375} = H$  and  $R^{376} = F$  and  $A^5 = -COOH$ , namely glutaminy-(3R,4R-fluoro-pyrrolidine-2S-carboxylic acid).
- (628) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = F$  and  $R^{372} = H$  and  $R^{375} = H$  and  $R^{376} = F$  and  $A^5 = -COOH$ , namely glutaminy-(3R,4S-fluoro-pyrrolidine-2S-carboxylic acid).
- (629) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = -H$  and  $R^{372} = -H$  and  $R^{375} = -F$  and  $R^{376} = -F$  and  $A^5 = -COOH$ , namely glutaminy-(3,3-difluoro-pyrrolidine-2S-carboxylic acid).
- (630) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = -F$  and  $R^{372} = -F$  and  $R^{375} = -F$  and  $R^{376} = -F$  and  $A^5 = -COOH$ , namely glutaminy-(3,3,4,4,-tetrafluoro-pyrrolidine-2S-carboxylic acid).
- (631) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = F$  and  $R^{372} = H$  and  $R^{375} = H$  and  $R^{376} = H$  and  $A^5 = -B(OH)_2$ , namely glutaminy-(4R-fluoro-pyrrolidine-2S-boronic acid).
- (632) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = H$  and  $R^{372} = F$  and  $R^{375} = H$  and  $R^{376} = H$  and  $A^5 = -B(OH)_2$ , namely glutaminy-(4S-fluoro-pyrrolidine-2S-boronic acid).

- (633) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = F$  and  $R^{372} = F$  and  $R^{375} = H$  and  $R^{376} = H$  and  $A^5 = -B(OH)_2$ , namely glutaminy-(4,4-difluoro-pyrrolidine-2-boronic acid).
- (634) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = H$  and  $R^{372} = H$  and  $R^{375} = F$  and  $R^{376} = H$  and  $A^5 = -B(OH)_2$ , namely glutaminy-(3S-fluoro-pyrrolidine-2S-boronic acid).
- (635) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = F$  and  $R^{372} = H$  and  $R^{375} = F$  and  $R^{376} = H$  and  $A^5 = -B(OH)_2$ , namely glutaminy-(3S,4R-difluoro-pyrrolidine-2S-boronic acid).
- (636) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = H$  and  $R^{372} = F$  and  $R^{375} = F$  and  $R^{376} = H$  and  $A^5 = -B(OH)_2$ , namely glutaminy-(3S,4S-difluoro-pyrrolidine-2S-boronic acid).
- (637) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = H$  and  $R^{372} = H$  and  $R^{375} = H$  and  $R^{376} = F$  and  $A^5 = -B(OH)_2$ , namely glutaminy-(3R-fluoro-pyrrolidine-2S-boronic acid).
- (638) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = H$  and  $R^{372} = F$  and  $R^{375} = H$  and  $R^{376} = F$  and  $A^5 = -B(OH)_2$ , namely glutaminy-(3R,4R-fluoro-pyrrolidine-2S-boronic acid).
- (639) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = F$  and  $R^{372} = H$  and  $R^{375} = H$  and  $R^{376} = F$  and  $A^5 = -B(OH)_2$ , namely glutaminy-(3R,4S-fluoro-pyrrolidine-2S-boronic acid).
- (640) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = -H$  and  $R^{372} = -H$  and  $R^{375} = -F$  and  $R^{376} = -F$  and  $A^5 = -B(OH)_2$ , namely glutaminy-(3,3-difluoro-pyrrolidine-2S-boronic acid).
- (641) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = -F$  and  $R^{372} = -F$  and  $R^{375} = -F$  and  $R^{376} = -F$  and  $A^5 = -B(OH)_2$ , namely glutaminy-(3,3,4,4-tetrafluoro-pyrrolidine-2S-boronic acid).
- (642) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = F$  and  $R^{372} = H$  and  $R^{375} = H$  and  $R^{376} = H$  and  $A^5 =$

-P(=O)(OR<sup>396</sup>)(OR<sup>397</sup>) and R<sup>396</sup> = -C<sub>6</sub>H<sub>5</sub> and R<sup>397</sup> = -C<sub>6</sub>H<sub>5</sub>, namely glutaminy-(4R-fluoro-pyrrolidine-2S-phosphonic acid diphenyl ester).

(643) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein R<sup>371</sup> = H and R<sup>372</sup> = F and R<sup>375</sup> = H and R<sup>376</sup> = H and A<sup>5</sup> = -P(=O)(OR<sup>396</sup>)(OR<sup>397</sup>) and R<sup>396</sup> = -C<sub>6</sub>H<sub>5</sub> and R<sup>397</sup> = -C<sub>6</sub>H<sub>5</sub>, namely glutaminy-(4S-fluoro-pyrrolidine-2S-phosphonic acid diphenyl ester).

(644) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein R<sup>371</sup> = F and R<sup>372</sup> = F and R<sup>375</sup> = H and R<sup>376</sup> = H and A<sup>5</sup> = -P(=O)(OR<sup>396</sup>)(OR<sup>397</sup>) and R<sup>396</sup> = -C<sub>6</sub>H<sub>5</sub> and R<sup>397</sup> = -C<sub>6</sub>H<sub>5</sub>, namely glutaminy-(4,4-difluoro-pyrrolidine-2S-phosphonic acid diphenyl ester).

(645) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein R<sup>371</sup> = H and R<sup>372</sup> = H and R<sup>375</sup> = F and R<sup>376</sup> = H and A<sup>5</sup> = -P(=O)(OR<sup>396</sup>)(OR<sup>397</sup>) and R<sup>396</sup> = -C<sub>6</sub>H<sub>5</sub> and R<sup>397</sup> = -C<sub>6</sub>H<sub>5</sub>, namely glutaminy-(3S-fluoro-pyrrolidine-2S-phosphonic acid diphenyl ester).

(646) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein R<sup>371</sup> = F and R<sup>372</sup> = H and R<sup>375</sup> = F and R<sup>376</sup> = H and A<sup>5</sup> = -P(=O)(OR<sup>396</sup>)(OR<sup>397</sup>) and R<sup>396</sup> = -C<sub>6</sub>H<sub>5</sub> and R<sup>397</sup> = -C<sub>6</sub>H<sub>5</sub>, namely glutaminy-(3S,4R-difluoro-pyrrolidine-2S-phosphonic acid diphenyl ester).

(647) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein R<sup>371</sup> = H and R<sup>372</sup> = F and R<sup>375</sup> = F and R<sup>376</sup> = H and A<sup>5</sup> = -P(=O)(OR<sup>396</sup>)(OR<sup>397</sup>) and R<sup>396</sup> = -C<sub>6</sub>H<sub>5</sub> and R<sup>397</sup> = -C<sub>6</sub>H<sub>5</sub>, namely glutaminy-(3S,4S-difluoro-pyrrolidine-2S-phosphonic acid diphenyl ester).

(648) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein R<sup>371</sup> = H and R<sup>372</sup> = H and R<sup>375</sup> = H and R<sup>376</sup> = F and A<sup>5</sup> = -P(=O)(OR<sup>396</sup>)(OR<sup>397</sup>) and R<sup>396</sup> = -C<sub>6</sub>H<sub>5</sub> and R<sup>397</sup> = -C<sub>6</sub>H<sub>5</sub>, namely glutaminy-(3R-fluoro-pyrrolidine-2S-phosphonic acid diphenyl ester).

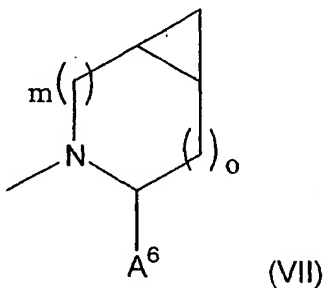
(649) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein R<sup>371</sup> = H and R<sup>372</sup> = F and R<sup>375</sup> = H and R<sup>376</sup> = F and A<sup>5</sup> = -P(=O)(OR<sup>396</sup>)(OR<sup>397</sup>) and R<sup>396</sup> = -C<sub>6</sub>H<sub>5</sub> and R<sup>397</sup> = -C<sub>6</sub>H<sub>5</sub>, namely glutaminy-(3R,4R-fluoro-pyrrolidine-2S-phosphonic acid diphenyl ester).

(650) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = F$  and  $R^{372} = H$  and  $R^{375} = H$  and  $R^{376} = F$  and  $A^5 = -P(=O)(OR^{396})(OR^{397})$  and  $R^{396} = -C_6H_5$  and  $R^{397} = -C_6H_5$ , namely glutaminyl-(3R,4S-fluoro-pyrrolidine-2S-phosphonic acid diphenyl ester).

(651) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = -H$  and  $R^{372} = -H$  and  $R^{375} = -F$  and  $R^{376} = -F$  and  $A^5 = -P(=O)(OR^{396})(OR^{397})$  and  $R^{396} = -C_6H_5$  and  $R^{397} = -C_6H_5$ , namely glutaminyl-(3,3-difluoro-pyrrolidine-2S-phosphonic acid diphenyl ester).

(652) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $R^{371} = -F$  and  $R^{372} = -F$  and  $R^{375} = -F$  and  $R^{376} = -F$  and  $A^5 = -P(=O)(OR^{396})(OR^{397})$  and  $R^{396} = -C_6H_5$  and  $R^{397} = -C_6H_5$ , namely glutaminyl-(3,3,4,4-tetrafluoro-pyrrolidine-2S-phosphonic acid diphenyl ester).

**Examples for prolin mimetics of formula (VII):**



(700) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $m = 0$  and  $o = 1$  and  $A^6 = -H$ , namely 1-glutaminyl-(4,5-methano-pyrrolidine).

(701) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $m = 1$  and  $o = 0$  and  $A^6 = -H$ , namely 1-glutaminyl-(3,4-methano-pyrrolidine).

- (702) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $m = 1$  and  $o = 1$  and  $A^6 = -H$ , namely 1-glutaminy-(4,5-methano-piperidine).
- (703) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $m = 0$  and  $o = 2$  and  $A^6 = -H$ , namely 1-glutaminy-(5,6-methano-piperidine).
- (704) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $m = 0$  and  $o = 1$  and  $A^6 = -C\equiv N$ , namely 1-glutaminy-(4,5-methano-pyrrolidin-2-carbonitrile).
- (705) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $m = 1$  and  $o = 0$  and  $A^6 = -C\equiv N$ , namely 1-glutaminy-(3,4-methano-pyrrolidin-2-carbonitrile).
- (706) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $m = 1$  and  $o = 1$  and  $A^6 = -C\equiv N$ , namely 1-glutaminy-(4,5-methano-piperidin-2-carbonitrile).
- (707) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $m = 0$  and  $o = 2$  and  $A^6 = -C\equiv N$ , namely 1-glutaminy-(5,6-methano-piperidin-2-carbonitrile).
- (708) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $m = 0$  and  $o = 1$  and  $A^6 = -COOH$ , namely 1-glutaminy-(4,5-methano-pyrrolidin-2-carboxylic acid).
- (709) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $m = 1$  and  $o = 0$  and  $A^6 = -COOH$ , namely 1-glutaminy-(3,4-methano-pyrrolidin-2-carboxylic acid).
- (710) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $m = 1$  and  $o = 1$  and  $A^6 = -COOH$ , namely 1-glutaminy-(4,5-methano-piperidin-2-carboxylic acid).
- (711) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $m = 0$  and  $o = 2$  and  $A^6 = -COOH$ , namely 1-glutaminy-(5,6-methano-piperidin-2-carboxylic acid).

(712) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $m = 0$  and  $o = 1$  and  $A^6 = -B(OH)_2$ , namely 1-glutaminy-(4,5-methano-pyrrolidin-2-boronic acid).

(713) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $m = 1$  and  $o = 0$  and  $A^6 = -B(OH)_2$ , namely 1-glutaminy-(3,4-methano-pyrrolidin-2-boronic acid).

(714) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $m = 1$  and  $o = 1$  and  $A^6 = -B(OH)_2$ , namely 1-glutaminy-(4,5-methano-piperidin-2-boronic acid).

(715) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $m = 0$  and  $o = 2$  and  $A^6 = -B(OH)_2$ , namely 1-glutaminy-(5,6-methano-piperidin-2-boronic acid).

(716) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $m = 0$  and  $o = 1$  and  $A^6 = -P(=O)(OR^{476})(OR^{477})$  and  $R^{476} = -C_6H_5$  and  $R^{477} = -C_6H_5$ , namely 1-glutaminy-(4,5-methano-pyrrolidin-2-phosphonic acid diphenyl ester).

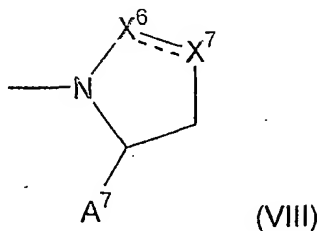
(717) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $m = 1$  and  $o = 0$  and  $A^6 = -P(=O)(OR^{476})(OR^{477})$  and  $R^{476} = -C_6H_5$  and  $R^{477} = -C_6H_5$ , namely 1-glutaminy-(3,4-methano-pyrrolidin-2-phosphonic acid diphenyl ester).

(718) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $m = 1$  and  $o = 1$  and  $A^6 = -P(=O)(OR^{476})(OR^{477})$  and  $R^{476} = -C_6H_5$  and  $R^{477} = -C_6H_5$ , namely 1-glutaminy-(4,5-methano-piperidin-2-phosphonic acid diphenyl ester).

(715) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $m = 0$  and  $o = 2$  and  $A^6 = -P(=O)(OR^{476})(OR^{477})$  and  $R^{476} = -C_6H_5$  and  $R^{477} = -C_6H_5$ , namely 1-glutaminy-(5,6-methano-piperidin-2-phosphonic acid diphenyl ester).



Examples for prolin mimetics of formula (VIII):



(800) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^6 = CR^{496}$  and  $R^{496} = H$  and  $X^7 = CR^{497}$  and  $R^{497} = H$  and  $X^6-X^7 = \text{double bond}$  and  $A^7 = -H$ , namely 1-glutaminy-(2,3-dihydro-1H-pyrrole).

(801) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^6 = N$  and  $X^7 = CR^{497}$  and  $R^{497} = H$  and  $X^6-X^7 = \text{double bond}$  and  $A^7 = -H$ , namely 1-glutaminy-(4,5-dihydro-1H-pyrazole).

(802) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^6 = CR^{496}$  and  $R^{496} = H$  and  $X^7 = N$  and  $X^6-X^7 = \text{double bond}$  and  $A^7 = -H$ , namely 1-glutaminy-(4,5-dihydro-1H-imidazole).

(803) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^6 = N$  and  $X^7 = N$  and  $X^6-X^7 = \text{double bond}$  and  $A^7 = -H$ , namely 1-glutaminy-(4,5-dihydro-1H-1,2,3-triazole).

(804) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^6 = O$  and  $X^7 = CR^{493}R^{494}$  and  $R^{493} = H$  and  $R^{494} = H$  and  $X^6-X^7 = \text{single bond}$  and  $A^7 = -H$ , namely 2-glutaminy-(isoxazolidine).

(805) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^6 = NR^{492}$  and  $R^{492} = H$  and  $X^7 = CR^{493}R^{494}$  and  $R^{493} = H$  and  $R^{494} = H$  and  $X^6-X^7 = \text{single bond}$  and  $A^7 = -H$ , namely 1-glutaminy-(pyrazolidine).

(806) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^6 = CR^{496}$  and  $R^{496} = H$  and  $X^7 = CR^{497}$  and  $R^{497} = H$  and

$X^6-X^7$  = double bond and  $A^7 = -C\equiv N$ , namely 1-glutaminy-(2,3-dihydro-1H-pyrrole-2-carbonitrile).

(807) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^6 = CR^{496}$  and  $R^{496} = -C\equiv N$  and  $X^7 = CR^{497}$  and  $R^{497} = H$  and  $X^6-X^7$  = double bond and  $A^7 = -H$ , namely 1-glutaminy-(4,5-dihydro-1H-pyrrole-2-carbonitrile).

(808) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^6 = N$  and  $X^7 = CR^{497}$  and  $R^{497} = H$  and  $X^6-X^7$  = double bond and  $A^7 = -C\equiv N$ , namely 1-glutaminy-(4,5-dihydro-1H-pyrazole-5-carbonitrile).

(809) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^6 = CR^{496}$  and  $R^{496} = H$  and  $X^7 = N$  and  $X^6-X^7$  = double bond and  $A^7 = -C\equiv N$ , namely 1-glutaminy-(4,5-dihydro-1H-imidazole-5-carbonitrile).

(810) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^6 = CR^{496}$  and  $R^{496} = -C\equiv N$  and  $X^7 = N$  and  $X^6-X^7$  = double bond and  $A^7 = -H$ , namely 1-glutaminy-(4,5-dihydro-1H-imidazole-2-carbonitrile).

(811) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^6 = N$  and  $X^7 = N$  and  $X^6-X^7$  = double bond and  $A^7 = -C\equiv N$ , namely 1-glutaminy-(4,5-dihydro-1H-1,2,3-triazole-5-carbonitrile).

(812) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^6 = O$  and  $X^7 = CR^{493}R^{494}$  and  $R^{493} = H$  and  $R^{494} = H$  and  $X^6-X^7$  = single bond and  $A^7 = -C\equiv N$ , namely 2-glutaminy-(isoxazolidine-3-carbonitrile).

(813) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^6 = NR^{492}$  and  $R^{492} = H$  and  $X^7 = CR^{493}R^{494}$  and  $R^{493} = H$  and  $R^{494} = H$  and  $X^6-X^7$  = single bond and  $A^7 = -C\equiv N$ , namely 1-glutaminy-(pyrazolidine-5-carbonitrile).

(814) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^6 = NR^{492}$  and  $R^{492} = -C\equiv N$  and  $X^7 = CR^{493}R^{494}$  and  $R^{493} = H$  and  $R^{494} = H$  and  $X^6-X^7$  = single bond and  $A^7 = H$ , namely 1-glutaminy-(pyrazolidine-2N-carbonitrile).

(815) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^6 = CR^{496}$  and  $R^{496} = H$  and  $X^7 = CR^{497}$  and  $R^{497} = H$  and  $X^6-X^7 = \text{double bond}$  and  $A^7 = -COOH$ , namely 1-glutaminy-(2,3-dihydro-1H-pyrrole-2-carboxylic acid).

(816) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^6 = CR^{496}$  and  $R^{496} = -COOH$ , and  $X^7 = CR^{497}$  and  $R^{497} = H$  and  $X^6-X^7 = \text{double bond}$  and  $A^7 = -H$ , namely 1-glutaminy-(4,5-dihydro-1H-pyrrole-2-carboxylic acid).

(817) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^6 = N$  and  $X^7 = CR^{497}$  and  $R^{497} = H$  and  $X^6-X^7 = \text{double bond}$  and  $A^7 = -COOH$ , namely 1-glutaminy-(4,5-dihydro-1H-pyrazole-5-carboxylic acid).

(818) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^6 = CR^{496}$  and  $R^{496} = H$  and  $X^7 = N$  and  $X^6-X^7 = \text{double bond}$  and  $A^7 = -COOH$ , namely 1-glutaminy-(4,5-dihydro-1H-imidazole-5-carboxylic acid).

(819) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^6 = CR^{496}$  and  $R^{496} = -COOH$  and  $X^7 = N$  and  $X^6-X^7 = \text{double bond}$  and  $A^7 = -H$ , namely 1-glutaminy-(4,5-dihydro-1H-imidazole-2-carboxylic acid).

(820) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^6 = N$  and  $X^7 = N$  and  $X^6-X^7 = \text{double bond}$  and  $A^7 = -COOH$ , namely 1-glutaminy-(4,5-dihydro-1H-1,2,3-triazole-5-carboxylic acid).

(821) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^6 = O$  and  $X^7 = CR^{493}R^{494}$  and  $R^{493} = H$  and  $R^{494} = H$  and  $X^6-X^7 = \text{single bond}$  and  $A^7 = -COOH$ , namely 2-glutaminy-(isoxazolidine-3-carboxylic acid).

(822) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^6 = NR^{492}$  and  $R^{492} = H$  and  $X^7 = CR^{493}R^{494}$  and  $R^{493} = H$  and  $R^{494} = H$  and  $X^6-X^7 = \text{single bond}$  and  $A^7 = -COOH$ , namely 1-glutaminy-(pyrazolidine-5-carboxylic acid).

- (823) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^6 = CR^{496}$  and  $R^{496} = H$  and  $X^7 = CR^{497}$  and  $R^{497} = H$  and  $X^6-X^7 = \text{double bond}$  and  $A^7 = -B(OH)_2$ , namely 1-glutaminy-(2,3-dihydro-1H-pyrrole-2-boronic acid).
- (824) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^6 = CR^{496}$  and  $R^{496} = -B(OH)_2$  and  $X^7 = CR^{497}$  and  $R^{497} = H$  and  $X^6-X^7 = \text{double bond}$  and  $A^7 = -H$ , namely 1-glutaminy-(4,5-dihydro-1H-pyrrole-2-boronic acid).
- (825) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^6 = N$  and  $X^7 = CR^{497}$  and  $R^{497} = H$  and  $X^6-X^7 = \text{double bond}$  and  $A^7 = -B(OH)_2$ , namely 1-glutaminy-(4,5-dihydro-1H-pyrazole-5-boronic acid).
- (826) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^6 = CR^{496}$  and  $R^{496} = H$  and  $X^7 = N$  and  $X^6-X^7 = \text{double bond}$  and  $A^7 = -B(OH)_2$ , namely 1-glutaminy-(4,5-dihydro-1H-imidazole-5-boronic acid).
- (827) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^6 = CR^{496}$  and  $R^{496} = -B(OH)_2$  and  $X^7 = N$  and  $X^6-X^7 = \text{double bond}$  and  $A^7 = -H$ , namely 1-glutaminy-(4,5-dihydro-1H-imidazole-2-boronic acid).
- (828) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^6 = N$  and  $X^7 = N$  and  $X^6-X^7 = \text{double bond}$  and  $A^7 = -B(OH)_2$ , namely 1-glutaminy-(4,5-dihydro-1H-1,2,3-triazole-5-boronic acid).
- (829) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^6 = O$  and  $X^7 = CR^{493}R^{494}$  and  $R^{493} = H$  and  $R^{494} = H$  and  $X^6-X^7 = \text{single bond}$  and  $A^7 = -B(OH)_2$ , namely 2-glutaminy-(isoxazolidine-3-boronic acid).
- (830) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^6 = NR^{492}$  and  $R^{492} = H$  and  $X^7 = CR^{493}R^{494}$  and  $R^{493} = H$  and  $R^{494} = H$  and  $X^6-X^7 = \text{single bond}$  and  $A^7 = -B(OH)_2$ , namely 1-glutaminy-(pyrazolidine-5-boronic acid).

(831) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^6 = CR^{496}$  and  $R^{496} = H$  and  $X^7 = CR^{497}$  and  $R^{497} = H$  and  $X^6-X^7 = \text{double bond}$  and  $A^7 = -P(=O)(OR^{556})(OR^{557})$  and  $R^{556} = -C_6H_5$  and  $R^{557} = -C_6H_5$ , namely 1-glutaminy-(2,3-dihydro-1H-pyrrole-2-phosphonic acid diphenyl ester).

(832) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^6 = CR^{496}$  and  $R^{496} = -P(=O)(OR^{516})(OR^{517})$  and  $R^{516} = -C_6H_5$  and  $R^{517} = -C_6H_5$  and  $X^7 = CR^{497}$  and  $R^{497} = H$  and  $X^6-X^7 = \text{double bond}$  and  $A^7 = -H$ , namely 1-glutaminy-(4,5-dihydro-1H-pyrrole-2-phosphonic acid diphenyl ester).

(833) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^6 = N$  and  $X^7 = CR^{497}$  and  $R^{497} = H$  and  $X^6-X^7 = \text{double bond}$  and  $A^7 = -P(=O)(OR^{556})(OR^{557})$  and  $R^{556} = -C_6H_5$  and  $R^{557} = -C_6H_5$ , namely 1-glutaminy-(4,5-dihydro-1H-pyrazole-5-phosphonic acid diphenyl ester).

(834) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^6 = CR^{496}$  and  $R^{496} = H$  and  $X^7 = N$  and  $X^6-X^7 = \text{double bond}$  and  $A^7 = -P(=O)(OR^{556})(OR^{557})$  and  $R^{556} = -C_6H_5$  and  $R^{557} = -C_6H_5$ , namely 1-glutaminy-(4,5-dihydro-1H-imidazole-5-phosphonic acid diphenyl ester).

(835) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^6 = CR^{496}$  and  $R^{496} = -P(=O)(OR^{516})(OR^{517})$  and  $R^{516} = -C_6H_5$  and  $R^{517} = -C_6H_5$  and  $X^7 = N$  and  $X^6-X^7 = \text{double bond}$  and  $A^7 = -H$ , namely 1-glutaminy-(4,5-dihydro-1H-imidazole-2-phosphonic acid diphenyl ester).

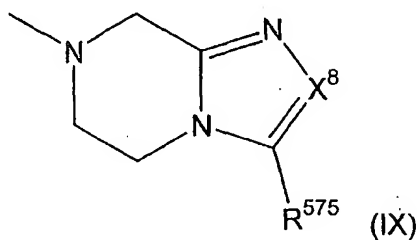
(836) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^6 = N$  and  $X^7 = N$  and  $X^6-X^7 = \text{double bond}$  and  $A^7 = -P(=O)(OR^{556})(OR^{557})$  and  $R^{556} = -C_6H_5$  and  $R^{557} = -C_6H_5$ , namely 1-glutaminy-(4,5-dihydro-1H-1,2,3-triazole-5-phosphonic acid diphenyl ester).

(837) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^6 = O$  and  $X^7 = CR^{493}R^{494}$  and  $R^{493} = H$  and  $R^{494} = H$  and  $X^6-X^7 = \text{single bond}$  and  $A^7 = -P(=O)(OR^{556})(OR^{557})$  and  $R^{556} = -C_6H_5$  and  $R^{557} = -C_6H_5$ , namely 2-glutaminy-(isoxazolidine-3-phosphonic acid diphenyl ester).

(838) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^6 = NR^{492}$  and  $R^{492} = H$  and  $X^7 = CR^{493}R^{494}$  and  $R^{493} = H$  and  $R^{494} = H$  and  $X^6-X^7 = \text{single bond}$  and  $A^7 = -P(=O)(OR^{556})(OR^{557})$  and  $R^{556} =$

$-\text{C}_6\text{H}_5$  and  $\text{R}^{557} = -\text{C}_6\text{H}_5$ , namely 1-glutaminy-(pyrazolidine-5-phosphonic acid diphenyl ester).

**Examples for prolin mimetics of formula (IX):**



(900) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $\text{X}^8 = \text{CR}^{570}$  and  $\text{R}^{570} = \text{H}$  and  $\text{R}^{575} = \text{H}$ , namely 7-glutaminy-(5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine).

(901) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $\text{X}^8 = \text{CR}^{570}$  and  $\text{R}^{570} = -\text{CH}_3$  and  $\text{R}^{575} = \text{H}$ , namely 7-glutaminy-(2-methyl-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine).

(902) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $\text{X}^8 = \text{CR}^{570}$  and  $\text{R}^{570} = -\text{CF}_3$  and  $\text{R}^{575} = \text{H}$ , namely 7-glutaminy-(2-(trifluoromethyl)-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine).

(903) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $\text{X}^8 = \text{CR}^{570}$  and  $\text{R}^{570} = -\text{CH}_2\text{CH}_3$  and  $\text{R}^{575} = \text{H}$ , namely 7-glutaminy-(2-ethyl-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine).

(904) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $\text{X}^8 = \text{CR}^{570}$  and  $\text{R}^{570} = -\text{C}_6\text{H}_5$  and  $\text{R}^{575} = \text{H}$ , namely 7-glutaminy-(2-phenyl-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine).

(905) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $\text{X}^8 = \text{CR}^{570}$  and  $\text{R}^{570} = -p\text{-C}_6\text{H}_4(\text{CF}_3)$  and  $\text{R}^{575} = \text{H}$ , namely 7-glutaminy-(2-(4-trifluoromethyl-phenyl)-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine).

(906) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -p-C_6H_5(CF_2CF_3)$  and  $R^{575} = H$ , namely 7-glutaminy-(2-(4-pentafluoroethyl-phenyl)-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine).

(907) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -C_6H_5(3-F)(4-CF_3)$  and  $R^{575} = H$ , namely 7-glutaminy-(2-(3-fluoro-4-trifluoromethyl-phenyl)-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine).

(908) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -p-C_6H_4F$  and  $R^{575} = H$ , namely 7-glutaminy-(2-(4-fluorophenyl)-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine).

(909) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -p-C_6H_4(OCH_3)$  and  $R^{575} = H$ , namely 7-glutaminy-(2-(4-methoxyphenyl)-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine).

(910) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -p-C_6H_4(OCF_3)$  and  $R^{575} = H$ , namely 7-glutaminy-(2-(4-(trifluoro-methoxy)-phenyl)-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine).

(911) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -p-C_6H_4(OCF_2CF_3)$  and  $R^{575} = H$ , namely 1-glutaminy-(2-(4-(pentafluoroethoxy)-phenyl)-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine).

(912) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -3,4-C_6H_3F_2$  and  $R^{575} = H$ , namely 7-glutaminy-(2-(3,4-difluoro-phenyl)-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine).

(913) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -CF_2CF_3$  and  $R^{575} = H$ , namely 7-glutaminy-(2-(pentafluoro-ethyl)-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine).

(914) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = H$  and  $R^{575} = -C\equiv N$ , namely 7-glutaminy-(3-cyano-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine).

(915) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -CH_3$  and  $R^{575} = -C\equiv N$ , namely 7-glutaminy-(2-methyl-3-cyano-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine).

(916) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -CF_3$  and  $R^{575} = -C\equiv N$ , namely 7-glutaminy-(2-(trifluoromethyl)-3-cyano-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine).

(917) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -CH_2CH_3$  and  $R^{575} = -C\equiv N$ , namely 7-glutaminy-(2-ethyl-3-cyano-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine).

(918) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -C_6H_5$  and  $R^{575} = -C\equiv N$ , namely 7-glutaminy-(2-phenyl-3-cyano-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine).

(919) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -p-C_6H_5(CF_3)$  and  $R^{575} = -C\equiv N$ , namely 7-glutaminy-(2-(4-trifluoromethyl-phenyl)-3-cyano-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine).

(920) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -p-C_6H_5(CF_2CF_3)$  and  $R^{575} = -C\equiv N$ , namely 7-glutaminy-(2-(4-pentafluoroethyl-phenyl)-3-cyano-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine).

(921) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -C_6H_5(3-F)(4-CF_3)$  and  $R^{575} = -C\equiv N$ , namely 7-glutaminy-(2-(3-fluoro-4-trifluoromethyl-phenyl)-3-cyano-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine).

(922) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -p-C_6H_4F$  and  $R^{575} = -C\equiv N$ , namely 7-glutaminy-(2-(4-fluorophenyl)-3-cyano-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine).

(923) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -p-C_6H_4(OCH_3)$  and  $R^{575} = -C\equiv N$ , namely 7-glutaminy-(2-(4-methoxyphenyl)-3-cyano-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine).



- (924) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -p-C_6H_4(OCF_3)$  and  $R^{575} = -C\equiv N$ , namely 7-glutaminy-(2-(4-(trifluoro-methoxy)-phenyl)-3-cyano-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine).
- (925) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -p-C_6H_4(OCF_2CF_3)$  and  $R^{575} = -C\equiv N$ , namely 1-glutaminy-(2-(4-(pentafluoroethoxy)-3-cyano-phenyl)-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine).
- (926) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -3,4-C_6H_3F_2$  and  $R^{575} = -C\equiv N$ , namely 7-glutaminy-(2-(3,4-difluoro-phenyl)-3-cyano-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine).
- (927) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -CF_2CF_3$  and  $R^{575} = -C\equiv N$ , namely 7-glutaminy-(2-(pentafluoro-ethyl)-3-cyano-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine).
- (928) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = H$  and  $R^{575} = -COOH$ , namely 7-glutaminy-(5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine-3-carboxylic acid).
- (929) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -CH_3$  and  $R^{575} = -COOH$ , namely 7-glutaminy-(2-methyl-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine-3-carboxylic acid).
- (930) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -CF_3$  and  $R^{575} = -COOH$ , namely 7-glutaminy-(2-(trifluoromethyl)-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine-3-carboxylic acid).
- (931) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -CH_2CH_3$  and  $R^{575} = -COOH$ , namely 7-glutaminy-(2-ethyl-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine-3-carboxylic acid).
- (932) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -C_6H_5$  and  $R^{575} = -COOH$ , namely 7-glutaminy-(2-phenyl-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine-3-carboxylic acid).

(933) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -p-C_6H_5(CF_3)$  and  $R^{575} = -COOH$ , namely 7-glutaminy-(2-(4-trifluoromethyl-phenyl)-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine-3-carboxylic acid).

(934) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -p-C_6H_5(CF_2CF_3)$  and  $R^{575} = -COOH$ , namely 7-glutaminy-(2-(4-pentafluoroethyl-phenyl)-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine-3-carboxylic acid).

(935) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -C_6H_5(3-F)(4-CF_3)$  and  $R^{575} = -COOH$ , namely 7-glutaminy-(2-(3-fluoro-4-trifluoromethyl-phenyl)-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine-3-carboxylic acid).

(936) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -p-C_6H_4F$  and  $R^{575} = -COOH$ , namely 7-glutaminy-(2-(4-fluorophenyl)-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine-3-carboxylic acid).

(937) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -p-C_6H_4(OCH_3)$  and  $R^{575} = -COOH$ , namely 7-glutaminy-(2-(4-methoxyphenyl)-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine-3-carboxylic acid).

(938) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -p-C_6H_4(OCF_3)$  and  $R^{575} = -COOH$ , namely 7-glutaminy-(2-(4-(trifluoro-methoxy)-phenyl)-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine-3-carboxylic acid).

(939) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -p-C_6H_4(OCF_2CF_3)$  and  $R^{575} = -COOH$ , namely 1-glutaminy-(2-(4-(pentafluoroethoxy)-phenyl)-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine-3-carboxylic acid).

(940) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -3,4-C_6H_3F_2$  and  $R^{575} = -COOH$ , namely 7-glutaminy-(2-(3,4-difluoro-phenyl)-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine-3-carboxylic acid).

(941) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -CF_2CF_3$  and  $R^{575} = -COOH$ , namely 7-glutaminy-(2-(pentafluoro-ethyl)-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine-3-carboxylic acid).

(942) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = H$  and  $R^{575} = -B(OH)_2$ , namely 7-glutaminy-(5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine-3-boronic acid).

(943) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -CH_3$  and  $R^{575} = -B(OH)_2$ , namely 7-glutaminy-(2-methyl-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine-3-boronic acid).

(944) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -CF_3$  and  $R^{575} = -B(OH)_2$ , namely 7-glutaminy-(2-(trifluoromethyl)-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine-3-boronic acid).

(945) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -CH_2CH_3$  and  $R^{575} = -B(OH)_2$ , namely 7-glutaminy-(2-ethyl-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine-3-boronic acid).

(946) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -C_6H_5$  and  $R^{575} = -B(OH)_2$ , namely 7-glutaminy-(2-phenyl-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine-3-boronic acid).

(947) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -p-C_6H_5(CF_3)$  and  $R^{575} = -B(OH)_2$ , namely 7-glutaminy-(2-(4-trifluoromethyl-phenyl)-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine-3-boronic acid).

(948) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -p-C_6H_5(CF_2CF_3)$  and  $R^{575} = -B(OH)_2$ , namely 7-glutaminy-(2-(4-pentafluoroethyl-phenyl)-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine-3-boronic acid).

(949) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -C_6H_5(3-F)(4-CF_3)$  and  $R^{575} = -B(OH)_2$ , namely 7-glutaminy-(2-(3-fluoro-4-trifluoromethyl-phenyl)-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine-3-boronic acid).

(950) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -p-C_6H_4F$  and  $R^{575} = -B(OH)_2$ , namely 7-glutaminy-(2-(4-fluorophenyl)-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine-3-boronic acid).

(951) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -p-C_6H_4(OCH_3)$  and  $R^{575} = -B(OH)_2$ , namely 7-glutaminy-(2-(4-methoxyphenyl)-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine-3-boronic acid).

(952) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -p-C_6H_4(OCF_3)$  and  $R^{575} = -B(OH)_2$ , namely 7-glutaminy-(2-(4-(trifluoro-methoxy)-phenyl)-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine-3-boronic acid).

(953) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -p-C_6H_4(OCF_2CF_3)$  and  $R^{575} = -B(OH)_2$ , namely 1-glutaminy-(2-(4-(pentafluoroethoxy)-phenyl)-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine-3-boronic acid).

(954) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -3,4-C_6H_3F_2$  and  $R^{575} = -B(OH)_2$ , namely 7-glutaminy-(2-(3,4-difluoro-phenyl)-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine-3-boronic acid).

(955) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -CF_2CF_3$  and  $R^{575} = -B(OH)_2$ , namely 7-glutaminy-(2-(pentafluoro-ethyl)-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine-3-boronic acid).

(956) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = H$  and  $R^{575} = -P(=O)(OR^{596})(OR^{597})$  and  $R^{596} = -C_6H_5$  and  $R^{597} = -C_6H_5$ , namely 7-glutaminy-(5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine-3-phosphonic acid diphenyl ester).

(957) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -CH_3$  and  $R^{575} = -P(=O)(OR^{596})(OR^{597})$  and  $R^{596} = -C_6H_5$  and  $R^{597} = -C_6H_5$ , namely 7-glutaminy-(2-methyl-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine-3-phosphonic acid diphenyl ester).

(958) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -CF_3$  and  $R^{575} = -P(=O)(OR^{596})(OR^{597})$  and  $R^{596} = -C_6H_5$  and  $R^{597} = -C_6H_5$ , namely 7-glutaminy-(2-(trifluoromethyl)-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine-3-phosphonic acid diphenyl ester).

(959) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -CH_2CH_3$  and  $R^{575} = -P(=O)(OR^{596})(OR^{597})$  and  $R^{596} = -C_6H_5$  and  $R^{597} = -C_6H_5$ , namely 7-glutaminy-(2-ethyl-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine-3-phosphonic acid diphenyl ester).

(960) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -C_6H_5$  and  $R^{575} = -P(=O)(OR^{596})(OR^{597})$  and  $R^{596} = -C_6H_5$  and  $R^{597} = -C_6H_5$ , namely 7-glutaminy-(2-phenyl-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine-3-phosphonic acid diphenyl ester).

(961) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -p-C_6H_5(CF_3)$  and  $R^{575} = -P(=O)(OR^{596})(OR^{597})$  and  $R^{596} = -C_6H_5$  and  $R^{597} = -C_6H_5$ , namely 7-glutaminy-(2-(4-trifluoromethyl-phenyl)-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine-3-phosphonic acid diphenyl ester).

(962) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -p-C_6H_5(CF_2CF_3)$  and  $R^{575} = -P(=O)(OR^{596})(OR^{597})$  and  $R^{596} = -C_6H_5$  and  $R^{597} = -C_6H_5$ , namely 7-glutaminy-(2-(4-pentafluoroethyl-phenyl)-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine-3-phosphonic acid diphenyl ester).

(963) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -C_6H_5(3-F)(4-CF_3)$  and  $R^{575} = -P(=O)(OR^{596})(OR^{597})$  and  $R^{596} = -C_6H_5$  and  $R^{597} = -C_6H_5$ , namely 7-glutaminy-(2-(3-fluoro-4-trifluoromethyl-phenyl)-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine-3-phosphonic acid diphenyl ester).

(964) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -p-C_6H_4F$  and  $R^{575} = -P(=O)(OR^{596})(OR^{597})$  and  $R^{596} = -C_6H_5$  and  $R^{597} = -C_6H_5$ , namely 7-glutaminy-(2-(4-

fluorophenyl)-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine-3-phosphonic acid diphenyl ester).

(965) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -p-C_6H_4(OCH_3)$  and  $R^{575} = -P(=O)(OR^{596})(OR^{597})$  and  $R^{596} = -C_6H_5$  and  $R^{597} = -C_6H_5$ , namely 7-glutaminy-(2-(4-methoxyphenyl)-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine-3-phosphonic acid diphenyl ester).

(966) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -p-C_6H_4(OCF_3)$  and  $R^{575} = -P(=O)(OR^{596})(OR^{597})$  and  $R^{596} = -C_6H_5$  and  $R^{597} = -C_6H_5$ , namely 7-glutaminy-(2-(4-(trifluoro-methoxy)-phenyl)-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine-3-phosphonic acid diphenyl ester).

(967) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -p-C_6H_4(OCF_2CF_3)$  and  $R^{575} = -P(=O)(OR^{596})(OR^{597})$  and  $R^{596} = -C_6H_5$  and  $R^{597} = -C_6H_5$ , namely 1-glutaminy-(2-(4-(pentafluoroethoxy)-phenyl)-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine-3-phosphonic acid diphenyl ester).

(968) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -3,4-C_6H_3F_2$  and  $R^{575} = -P(=O)(OR^{596})(OR^{597})$  and  $R^{596} = -C_6H_5$  and  $R^{597} = -C_6H_5$ , namely 7-glutaminy-(2-(3,4-difluoro-phenyl)-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine-3-phosphonic acid diphenyl ester).

(969) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -CF_2CF_3$  and  $R^{575} = -P(=O)(OR^{596})(OR^{597})$  and  $R^{596} = -C_6H_5$  and  $R^{597} = -C_6H_5$ , namely 7-glutaminy-(2-(pentafluoro-ethyl)-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine-3-phosphonic acid diphenyl ester).

(970) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -H$  and  $R^{575} = -C_6H_5$ , namely 7-glutaminy-(3-phenyl-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine).

- (971) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -H$  and  $R^{575} = -CH_2C_6H_5$ , namely 7-glutaminy-(3-benzyl-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine).
- (972) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = CR^{570}$  and  $R^{570} = -H$  and  $R^{575} = 2H\text{-tetrazol-5-yl}$ , namely 7-glutaminy-(3-(2H-tetrazol-5-yl)-5,6,7,8-tetrahydro(imidazo[1,2-a]pyrazine).
- (973) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = N$  and  $R^{575} = -H$ , namely 7-glutaminy-(5,6,7,8-tetrahydro-1,2,4-triazolo[4,3-a]pyrazine).
- (974) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = N$  and  $R^{575} = -CH_3$ , namely 7-glutaminy-(3-methyl-5,6,7,8-tetrahydro-1,2,4-triazolo[4,3-a]pyrazine).
- (975) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = N$  and  $R^{575} = -CH_2CH_3$ , namely 7-glutaminy-(3-ethyl-5,6,7,8-tetrahydro-1,2,4-triazolo[4,3-a]pyrazine).
- (976) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = N$  and  $R^{575} = -CF_3$ , namely 7-glutaminy-(3-trifluoromethyl-5,6,7,8-tetrahydro-1,2,4-triazolo[4,3-a]pyrazine).
- (977) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = N$  and  $R^{575} = -CF_2CF_3$ , namely 7-glutaminy-(3-pentafluoroethyl-5,6,7,8-tetrahydro-1,2,4-triazolo[4,3-a]pyrazine).
- (978) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = N$  and  $R^{575} = -C_6H_5$ , namely 7-glutaminy-(3-phenyl-5,6,7,8-tetrahydro-1,2,4-triazolo[4,3-a]pyrazine).
- (979) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = N$  and  $R^{575} = -C_6H_4(4-F)$ , namely 7-glutaminy-(3-(4-fluoro-phenyl)-5,6,7,8-tetrahydro-1,2,4-triazolo[4,3-a]pyrazine).
- (980) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = N$  and  $R^{575} = -C_6H_4(4-CF_3)$ , namely 7-glutaminy-(3-(4-trifluoromethyl-phenyl)-5,6,7,8-tetrahydro-1,2,4-triazolo[4,3-a]pyrazine).

(981) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = N$  and  $R^{575} = -C_6H_3(3-F)(4-CF_3)$ , namely 7-glutaminy-(3-(3-fluoro-4-trifluoromethyl-phenyl)-5,6,7,8-tetrahydro-1,2,4-triazolo[4,3-a]pyrazine).

(982) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = N$  and  $R^{575} = -CH_2CF_3$ , namely 7-glutaminy-(3-(2,2,2-trifluoro-eth-1-yl)-5,6,7,8-tetrahydro-1,2,4-triazolo[4,3-a]pyrazine).

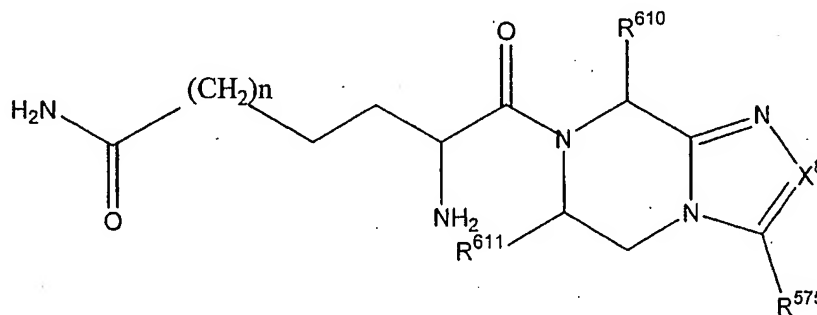
(983) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = N$  and  $R^{575} = -C\equiv N$ , namely 7-glutaminy-(3-cyano-5,6,7,8-tetrahydro-1,2,4-triazolo[4,3-a]pyrazine).

(984) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = N$  and  $R^{575} = -COOH$ , namely 7-glutaminy-(5,6,7,8-tetrahydro-1,2,4-triazolo[4,3-a]pyrazine-3-carboxylic acid).

(985) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = N$  and  $R^{575} = -B(OH)_2$ , namely 7-glutaminy-(5,6,7,8-tetrahydro-1,2,4-triazolo[4,3-a]pyrazine-3-boronic acid).

(986) Compound according to general formula (I) containing L- $\alpha$ -glutamine or L- $\alpha$ -homoglutamine, wherein  $X^8 = N$  and  $R^{575} = -P(=O)(OR^{596})(OR^{597})$  and  $R^{596} = -C_6H_5$  and  $R^{597} = -C_6H_5$ , namely 7-glutaminy-(5,6,7,8-tetrahydro-1,2,4-triazolo[4,3-a]pyrazine-3-phosphonic acid diphenyl ester).

#### Examples for prolin mimetics of formula (IXa):



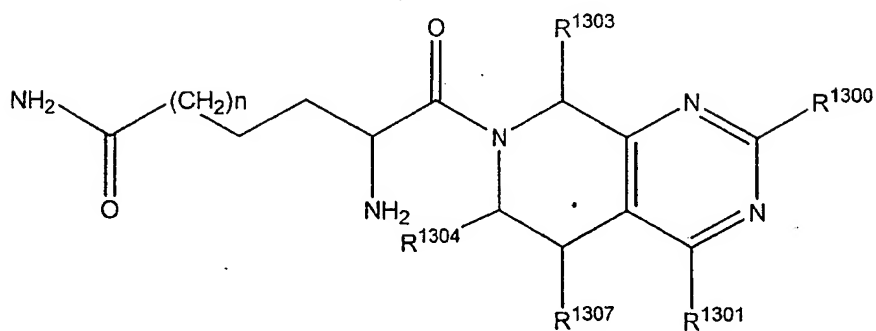
(IXa)



Ex.	n	R <sup>610</sup>	R <sup>611</sup>	X <sup>8</sup>	R <sup>575</sup>
1000	0	4-F-C <sub>6</sub> H <sub>4</sub>	H	C-CF <sub>3</sub>	H
1001	1	4-F- C <sub>6</sub> H <sub>4</sub>	H	C-CF <sub>3</sub>	H
1002	0	3-(CF <sub>3</sub> )C <sub>6</sub> H <sub>4</sub>	H	C-CF <sub>3</sub>	H
1003	1	3-(CF <sub>3</sub> )C <sub>6</sub> H <sub>4</sub>	H	C-CF <sub>3</sub>	H
1005	0	Me	H	C-CF <sub>3</sub>	H
1006	1	Me	H	C-CF <sub>3</sub>	H
1007	0	Et	H	C-CF <sub>3</sub>	H
1008	1	Et	H	C-CF <sub>3</sub>	H
1009	0	Isopropyl	H	C-CF <sub>3</sub>	H
1010	1	Isopropyl	H	C-CF <sub>3</sub>	H
1011	0	H	4-F-C <sub>6</sub> H <sub>4</sub>	C-CF <sub>3</sub>	H
1012	1	H	4-F-C <sub>6</sub> H <sub>4</sub>	C-CF <sub>3</sub>	H
1013	0	H	Me	C-CF <sub>3</sub>	H
1014	1	H	Me	C-CF <sub>3</sub>	H
1015	0	H	3-(CF <sub>3</sub> )C <sub>6</sub> H <sub>4</sub>	C-CF <sub>3</sub>	H
1016	1	H	3-(CF <sub>3</sub> )C <sub>6</sub> H <sub>4</sub>	C-CF <sub>3</sub>	H
1017	0	Et	H	N	CF <sub>3</sub>
1018	1	Et	H	N	CF <sub>3</sub>
1019	0	Me	H	N	CF <sub>3</sub>
1020	1	Me	H	N	CF <sub>3</sub>
1021	0	H	Et-C <sub>6</sub> H <sub>4</sub>	CH	Me
1022	1	H	Et- C <sub>6</sub> H <sub>4</sub>	CH	Me
1023	0	H	Et- C <sub>6</sub> H <sub>4</sub>	N	Me
1024	1	H	Et- C <sub>6</sub> H <sub>4</sub>	N	Me
1025	0	Me	H	N	Me
1026	1	Me	H	N	Me
1027	0	Me	H	C-CF <sub>3</sub>	H
1028	1	Me	H	C-CF <sub>3</sub>	H

1029	0	4-F-C <sub>6</sub> H <sub>4</sub>	H	C-CF <sub>3</sub>	H
1030	1	4-F-C <sub>6</sub> H <sub>4</sub>	H	C-CF <sub>3</sub>	H
1031	0	CO <sub>2</sub> Me	H	C-CF <sub>3</sub>	H
1032	1	CO <sub>2</sub> Me	H	C-CF <sub>3</sub>	H
1033	0	H	Me	N	Me
1034	1	H	Me	N	Me
1035	0	Me	Me	N	Me
1036	1	Me	Me	N	Me

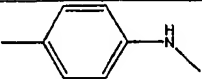
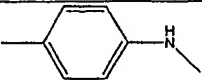
Examples for prolin mimetics of formula (XIII):



(XIII)

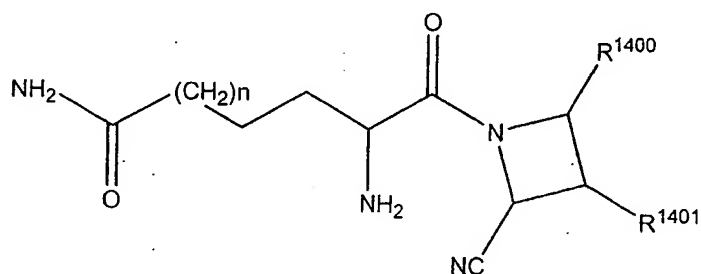
Ex.	n	R <sup>1300</sup>	R <sup>1301</sup>	R <sup>1303</sup>	R <sup>1304</sup>	R <sup>1307</sup>
1200	0	CF <sub>3</sub>	H	H	H	H
1201	1	CF <sub>3</sub>	H	H	H	H
1203	0	CF <sub>3</sub>	OCHMe <sub>2</sub>	H	H	H
1204	1	CF <sub>3</sub>	OCHMe <sub>2</sub>	H	H	H
1205	0	CF <sub>3</sub>	NHMe	H	H	H
1206	1	CF <sub>3</sub>	NHMe	H	H	H

1207	0	4-(CF <sub>3</sub> )C <sub>6</sub> H <sub>4</sub>	OH	H	H	H
1208	1	4-(CF <sub>3</sub> )C <sub>6</sub> H <sub>4</sub>	OH	H	H	H
1209	0	4-F-C <sub>6</sub> H <sub>4</sub>	H	H	H	H
1210	1	4-F-C <sub>6</sub> H <sub>4</sub>	H	H	H	H
1211	0	H	H	H	H	H
1212	1	H	H	H	H	H
1213	0	3-Pyridyl	H	H	H	H
1214	1	3-Pyridyl	H	H	H	H
1215	0	Me	H	H	H	H
1216	1	Me	H	H	H	H
1217	0	3-F-C <sub>6</sub> H <sub>4</sub>	H	H	H	H
1218	1	3-F-C <sub>6</sub> H <sub>4</sub>	H	H	H	H
1219	0	Ph	H	H	H	H
1220	1	Ph	H	H	H	H
1221	0	NMe <sub>2</sub>	H	H	H	H
1222	1	NMe <sub>2</sub>	H	H	H	H
1223	0	4-morpholino	H	H	H	H
1224	1	4-morpholino	H	H	H	H
1225	0	4-(OCF <sub>3</sub> )C <sub>6</sub> H <sub>4</sub>	H	H	H	H
1226	1	4-(OCF <sub>3</sub> )C <sub>6</sub> H <sub>4</sub>	H	H	H	H
1227	0	Cyclopropyl	H	H	H	H
1228	1	Cyclopropyl	H	H	H	H
1229	0	4-(NMe <sub>2</sub> )C <sub>6</sub> H <sub>4</sub>	H	H	H	H
1230	1	4-(NMe <sub>2</sub> )C <sub>6</sub> H <sub>4</sub>	H	H	H	H
1231	0	4-pyridyl	H	H	H	H
1232	1	4-pyridyl	H	H	H	H
1233	0	4-(SO <sub>2</sub> Me)C <sub>6</sub> H <sub>4</sub>	H	H	H	H
1234	1	4-(SO <sub>2</sub> Me)C <sub>6</sub> H <sub>4</sub>	H	H	H	H
1235	0	3-Me-4-NO <sub>2</sub> - imidazol-2-yl	H	H	H	H
1236	1	3-Me-4-NO <sub>2</sub> -	H	H	H	H

		imidazol-2-yl				
1237	0	4-(SO <sub>2</sub> CF <sub>3</sub> )C <sub>6</sub> H <sub>4</sub>	H	H	H	H
1238	1	4-(SO <sub>2</sub> CF <sub>3</sub> )C <sub>6</sub> H <sub>4</sub>	H	H	H	H
1239	0	4-(SO <sub>2</sub> NH <sub>2</sub> )C <sub>6</sub> H <sub>4</sub>	H	H	H	H
1240	1	4-(SO <sub>2</sub> NH <sub>2</sub> )C <sub>6</sub> H <sub>4</sub>	H	H	H	H
1241	0		H	H	H	H
1242	1		H	H	H	H
1243	0	2-pyrazinyl	H	H	H	H
1244	1	2-pyrazinyl	H	H	H	H
1245	0	CF <sub>3</sub>	H	Me	H	H
1246	1	CF <sub>3</sub>	H	Me	H	H
1247	0	4-Me-C <sub>6</sub> H <sub>4</sub>	H	H	H	H
1248	1	4-Me-C <sub>6</sub> H <sub>4</sub>	H	H	H	H
1249	0	3,4-(Cl) <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	H	H	H	H
1250	1	3,4-(Cl) <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	H	H	H	H
1251	0	4-Cl-C <sub>6</sub> H <sub>4</sub>	H	H	H	H
1252	1	4-Cl-C <sub>6</sub> H <sub>4</sub>	H	H	H	H
1253	0	2-Cl-C <sub>6</sub> H <sub>4</sub>	H	H	H	H
1254	1	2-Cl-C <sub>6</sub> H <sub>4</sub>	H	H	H	H
1255	0	2-F-C <sub>6</sub> H <sub>4</sub>	H	H	H	H
1256	1	2-F-C <sub>6</sub> H <sub>4</sub>	H	H	H	H
1257	0	2-pyridyl	H	H	H	H
1258	1	2-pyridyl	H	H	H	H
1259	0	4-(CONH <sub>2</sub> )C <sub>6</sub> H <sub>4</sub>	H	H	H	H
1260	1	4-(CONH <sub>2</sub> )C <sub>6</sub> H <sub>4</sub>	H	H	H	H
1261	0	2-pyrazinyl	CF <sub>3</sub>	H	H	H
1262	1	2-pyrazinyl	CF <sub>3</sub>	H	H	H
1263	0	4-(NH <sub>2</sub> )C <sub>6</sub> H <sub>4</sub>	H	H	H	H
1264	1	4-(NH <sub>2</sub> )C <sub>6</sub> H <sub>4</sub>	H	H	H	H

1265	0	H	CF <sub>3</sub>	H	H	H
1266	1	H	CF <sub>3</sub>	H	H	H
1267	0	4-(SO <sub>2</sub> Me)C <sub>6</sub> H <sub>4</sub>	CF <sub>3</sub>	H	H	H
1268	1	4-(SO <sub>2</sub> Me)C <sub>6</sub> H <sub>4</sub>	CF <sub>3</sub>	H	H	H
1269	0	4-(NHSO <sub>2</sub> Me)C <sub>6</sub> H <sub>4</sub>	H	H	H	H
1270	1	4-(NHSO <sub>2</sub> Me)C <sub>6</sub> H <sub>4</sub>	H	H	H	H

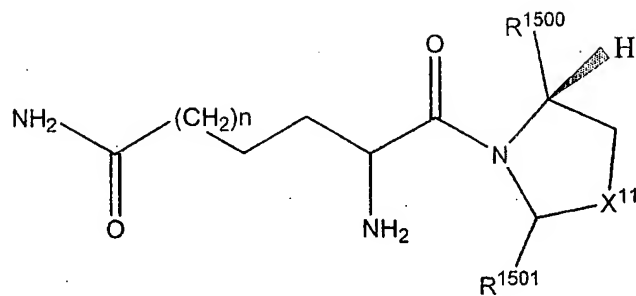
Examples for prolin mimetics of formula (XIV):



(XIV)

Ex.	n	R <sup>1400</sup>	R <sup>1401</sup>
1300	0	H	H
1301	1	H	H
1302	0	H	F
1303	1	H	F

Examples for prolin mimetics of formula (XV):

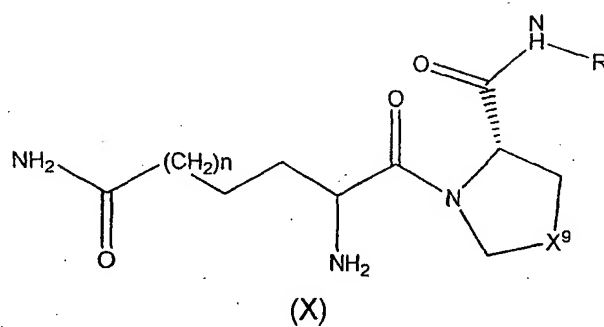


(XV)

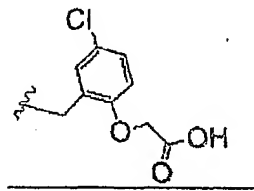
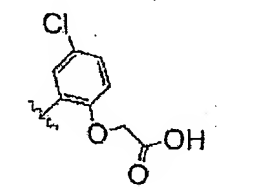
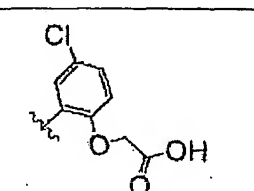
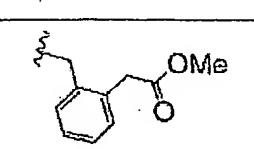
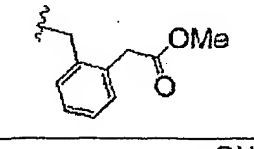


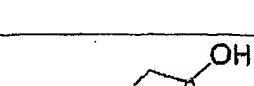

Ex.	n	R <sup>1500</sup>	R <sup>1501</sup>	X <sup>11</sup>
1400	0	CN	Me	CH <sub>2</sub>
1401	1	CN	Me	CH <sub>2</sub>
1402	0	CN	Me	CHF
1403	1	CN	Me	CHF
1404	0	CN	Me	CF <sub>2</sub>
1405	1	CN	Me	CF <sub>2</sub>
1406	0	CN	Et	CH <sub>2</sub>
1407	1	CN	Et	CH <sub>2</sub>
1408	0	CN	Et	CHF
1409	1	CN	Et	CHF
1410	0	CN	Et	CF <sub>2</sub>
1411	1	CN	Et	CF <sub>2</sub>
1412	0	CN	Ethynyl	CH <sub>2</sub>
1413	1	CN	Ethynyl	CH <sub>2</sub>
1414	0	CN	Ethynyl	CHF
1415	1	CN	Ethynyl	CHF
1416	0	CN	Ethynyl	CF <sub>2</sub>
1417	1	CN	Ethynyl	CF <sub>2</sub>

1418	0	CN	Vinyl	CH <sub>2</sub>
1419	1	CN	Vinyl	CH <sub>2</sub>
1420	0	CN	Vinyl	CHF
1421	1	CN	Vinyl	CHF
1422	0	CN	Vinyl	CF <sub>2</sub>
1423	1	CN	Vinyl	CF <sub>2</sub>
1424	0	CN	Prop-1-ynyl	CH <sub>2</sub>
1425	1	CN	Prop-1-ynyl	CH <sub>2</sub>
1426	0	CN	Prop-1-ynyl	CHF
1427	1	CN	Prop-1-ynyl	CHF
1428	0	CN	Prop-1-ynyl	CF <sub>2</sub>
1429	1	CN	Prop-1-ynyl	CF <sub>2</sub>

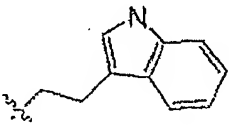
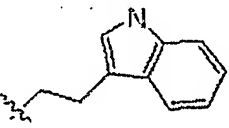
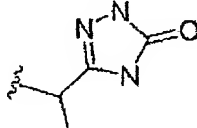
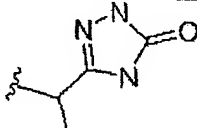
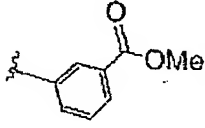
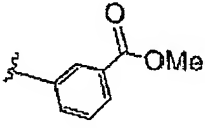
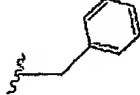
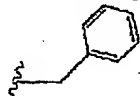
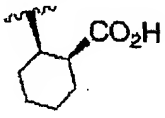
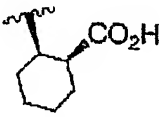
Examples for prolin mimetics of formula (X):

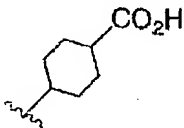
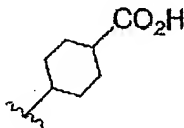
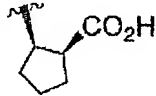
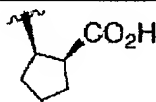
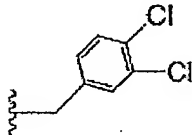
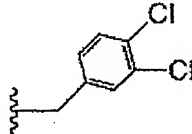
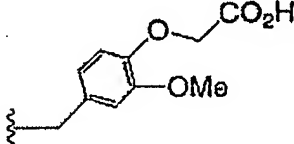
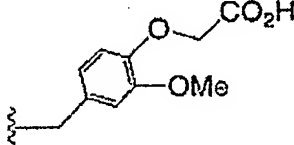


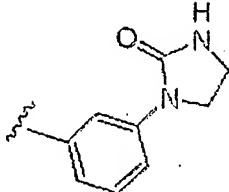
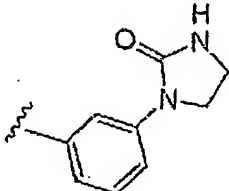
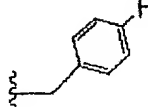
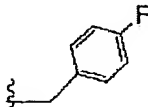
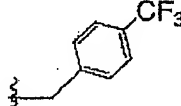
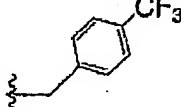
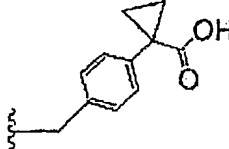
Ex.	n	X <sup>9</sup>	R
1500	0	S	

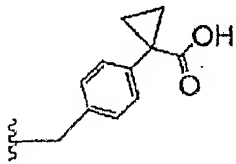
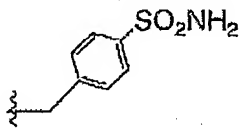
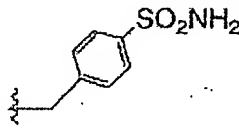
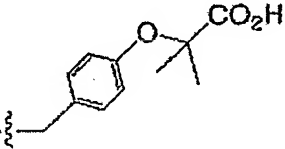
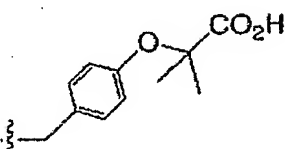
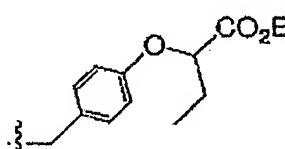
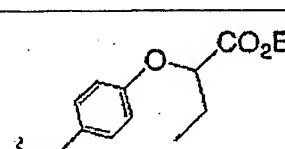
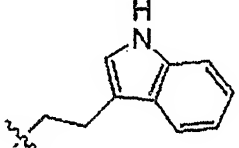
1501	1	S	 <chem>CC(=O)Oc1ccc(Cl)cc1CO</chem>
1502	0	CH <sub>2</sub>	 <chem>CC(=O)Oc1ccc(Cl)cc1CO</chem>
1503	1	CH <sub>2</sub>	 <chem>CC(=O)Oc1ccc(Cl)cc1CO</chem>
1504	0	S	 <chem>CC(=O)Oc1ccccc1COC(=O)Cc2ccccc2</chem>
1505	1	S	 <chem>CC(=O)Oc1ccccc1COC(=O)Cc2ccccc2</chem>
1506	0	CH <sub>2</sub>	 <chem>OC(=O)CCCCC=O</chem>
1507	1	CH <sub>2</sub>	 <chem>OC(=O)CCCCC=O</chem>
1508	0	S	 <chem>OC(=O)CCCCC=O</chem>
1509	1	S	 <chem>OC(=O)CCCCC=O</chem>

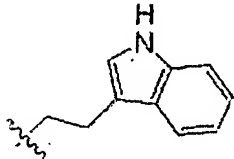
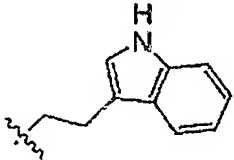
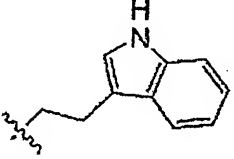


1510	0	CH <sub>2</sub>	
1511	1	CH <sub>2</sub>	
1512	0	CH <sub>2</sub>	
1513	1	CH <sub>2</sub>	
1514	0	CH <sub>2</sub>	
1515	1	CH <sub>2</sub>	
1516	0	CH <sub>2</sub>	
1517	1	CH <sub>2</sub>	
1518	0	CH <sub>2</sub>	
1519	1	CH <sub>2</sub>	

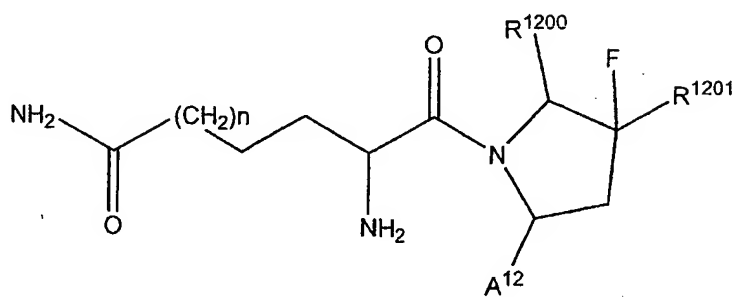
1520	0	CH <sub>2</sub>	
1521	1	CH <sub>2</sub>	
1522	0	CH <sub>2</sub>	
1523	1	CH <sub>2</sub>	
1524	0	CH <sub>2</sub>	
1525	1	CH <sub>2</sub>	
1526	0	CH <sub>2</sub>	
1527	1	CH <sub>2</sub>	

1528	0	CH <sub>2</sub>	
1529	1	CH <sub>2</sub>	
1530	0	CH <sub>2</sub>	
1531	1	CH <sub>2</sub>	
1532	0	CH <sub>2</sub>	
1533	1	CH <sub>2</sub>	
1534	0	CH <sub>2</sub>	

1535	1	CH <sub>2</sub>	
1536	0	CH <sub>2</sub>	
1537	1	CH <sub>2</sub>	
1538	0	CH <sub>2</sub>	
1539	1	CH <sub>2</sub>	
1540	0	S	
1541	1	S	
1542	0	CH <sub>2</sub>	

1543	1	CH <sub>2</sub>	
1544	0	S	
1545	1	S	

Examples for prolin mimetics of formula (XII):

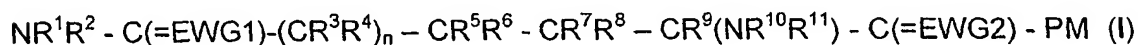


(XII)

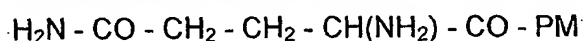
**Examples for prolin mimetics of formula (XII):**

Ex.	n	R <sup>1200</sup>	R <sup>1201</sup>	A <sup>12</sup>
1600	0	H	F	CN
1601	1	H	F	CN
1602	0	H	F	H
1603	1	H	F	H
1604	0	H	H	H
1605	1	H	H	H
1606	0	CN	F	H
1607	1	CN	F	H

The present invention provides a compound of the formula



and especially of the formula

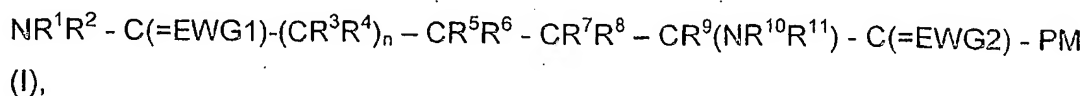


or a pharmaceutically acceptable salt thereof.

The present invention therefore provides a method of treating a condition mediated by modulation of the DPIV or DPIV – like enzyme activity in a subject in need thereof which comprises administering any of the compounds of the present invention or pharmaceutical compositions thereof in a quantity and dosing regimen therapeutically effective to treat the condition. Additionally, the present invention includes the use of the compounds of the present invention, and their corresponding pharmaceutically acceptable acid addition salt forms, for the preparation of a medicament for the prevention or treatment of a condition mediated by modulation of the DPIV activity in a subject.

**Indications:**

In view of their ability to inhibit DPIV and DPIV – like enzyme activity, the compounds of the present invention, especially the compounds of general formula (I)



and their corresponding pharmaceutically acceptable acid addition salt forms, are useful for the preparation of a medicament for the treatment of conditions mediated respectively modulated by said enzyme activities in mammals.

Additionally, the capability of the glutaminy cyclase to control the half life period of the DP IV inhibitor containing a N-terminal glutaminy or homoglutaminy residue, respectively, is useful for the preparation of a medicament to definitely control the time of action of the simultaneously administrated DPIV inhibitor. Therefore, the simultaneous administration of both the DPIV inhibitor and the QC inhibitor can be used for the treating conditions mediated respectively modulated by DP IV or DP IV like enzyme activities in mammals for a distinct period of time.

Therefore, the DP IV inhibitors, optionally combined with the QC inhibitors, both disclosed therein, are useful for the preparation of a medicament for the treatment in order to prevent or to alleviate pathological metabolic abnormalities of mammals, preferably of humans, which are related to DP IV or DP IV-like enzyme activity.

Especially, these diseases comprise

**metabolic diseases** like impaired glucose tolerance, impaired fasting glucose, impaired glucose metabolism, prediabetes, glucosuria, hyperlipidemia, metabolic acidosis, diabetes mellitus, non-insulin dependent diabetes mellitus, diabetic neuropathy and nephropathy and of sequelae caused by diabetes mellitus and obesity;

**neurodegenerative diseases**; high blood pressure and disturbance of signal action at the cells of the islets of Langerhans and insulin sensitivity in the peripheral tissue

in the postprandial phase; the metabolism-related hypertension and cardiovascular sequelae caused by hypertension;

**dermal diseases** like skin diseases and diseases of the mucosae;

**immune and autoimmune disorders**, multiple sclerosis, and inflammatory conditions; arthritis; obesity; allograft transplantation; cancer,;

**neuronal disorders as well as psychosomatic, neuropsychiatric and depressive illnesses**, such as anxiety, depression, sleep disorders, chronic fatigue, schizophrenia, epilepsy, nutritional disorders, spasm and chronic pain.

The indications above refer each to both acute and chronic form of the disease.

In a more preferred embodiment of this invention, the compounds of the present invention and their corresponding pharmaceutically acceptable acid addition salt forms, improve glucose tolerance by lowering elevated blood glucose levels in response to an oral glucose challenge and, therefore, are useful in treating **non-insulin-dependent diabetes mellitus (type 2 diabetes mellitus)**. The DP IV inhibitors of the present invention are especially used for lowering the blood glucose levels below the glucose concentration characteristic of hyperglycemia in the serum of a mammal, especially of a human, in the case of non-insulin dependent diabetes mellitus.

The compounds and combinations of the present invention are especially useful for the treatment of pathological states, selected from the group consisting of IGT, IFG and IGM, which are characteristic for the prediabetic state.

#### **Galenic preparations and formulations:**

The compounds of the present invention can be converted into acid addition salts, especially pharmaceutically acceptable acid addition salts.

The method of treating conditions modulated by dipeptidyl peptidase IV and DP-IV-like enzymes described in the present invention may also be carried out using a pharmaceutical composition comprising one or more of the compounds as defined



herein and a **pharmaceutically acceptable carrier**. Therefore, the present invention provides, in a further embodiment, **formulations** for the compounds of the present invention, and their corresponding pharmaceutically acceptable acid addition salt forms, in pharmaceutical compositions.

Preferably these compositions are in **unit dosage forms** from such as tablets, pills, capsules, powders, granules, sterile parenteral solutions or suspensions, metered aerosol or liquid sprays, drops, ampoules, autoinjector devices or suppositories. The compound may be administered to a patient by any conventional route of administration, including, but not limited to, intravenous, oral, subcutaneous, intramuscular, intradermal, parenteral, intranasal, sublingual or rectal administration, or for administration by inhalation or insufflation.

Compounding techniques: To prepare the pharmaceutical compositions of this invention, one or more compounds of the present invention, especially the DP IV inhibitors according to general formula (I) of the present invention, as well as optionally, the inhibitors of glutaminy cyclase, and their corresponding pharmaceutically acceptable acid addition salt forms, as the active ingredients, are intimately admixed with a pharmaceutical carrier according to conventional pharmaceutical compounding techniques, which carrier may take a wide variety of forms depending of the form of preparation desired for administration. Compounds of the present invention may also be coupled with soluble polymers as targetable drug carriers.

Homogeneous preparation: For preparing solid compositions such as tablets, the principal active ingredient is ideally mixed with a pharmaceutical carrier, e.g. conventional tableting ingredients such as corn starch, lactose, sucrose, sorbitol, talc, stearic acid, magnesium stearate, dicalcium phosphate or gums, and other pharmaceutical diluents, e.g. water, to form a solid preformulation composition containing a homogeneous mixture of a compound of the present invention, or a pharmaceutically acceptable salt thereof. When referring to these preformulation compositions as homogeneous, it is meant that the active ingredient is ideally

dispersed evenly throughout the composition so that the composition may be readily subdivided into equally effective dosage forms such as tablets, pills and capsules. This solid preformulation composition may then be subdivided into unit dosage forms of the type described above containing from about 0.1 to about 1000 mg, preferably from about 5 to about 500 mg of the active ingredient of the present invention.

Concentration and content of active agent: The pharmaceutical compositions herein will contain, per dosage unit, e.g., tablet, capsule, powder, injection, suppository, teaspoonful and the like, of from about 0.01 mg to about 1000 mg (preferably about 5 to about 500 mg) and may be given at a dosage of from about 0.1 to about 300 mg/kg bodyweight per day (preferably 1 to 50 mg/kg per day).

Oral dosage forms: In preparing the compositions in oral dosage form, any of the usual pharmaceutical media may be employed. Compositions suitable for oral administration include solid forms, such as pills, tablets, caplets, capsules (each including immediate release, timed release and sustained release formulations), granules, and powders. For solid oral preparations such as, for example, powders, capsules, gelcaps and tablets, suitable carriers and additives may advantageously include starches, sugars, diluents, granulating agents, lubricants, binders, disintegrating agents and the like. More preferably, for oral administration in the form of a tablet or capsule, the active drug component can be combined with an oral, non-toxic pharmaceutically acceptable inert carrier such as ethanol, glycerol, water and the like.

Coating of tablets, pills and capsules: Because of their ease in administration, tablets, pills and capsules represent the most advantageous oral dosage unit form, in which case solid pharmaceutical carriers are employed. If desired, the tablets, pills or capsules of the novel composition can be advantageously sugar coated or enteric coated by standard techniques or otherwise compounded to provide a dosage form affording the advantage of prolonged action. For example, the tablet or pill can comprise an inner dosage and an outer dosage component, the latter being in the form of an envelope over the former. The two components can be separated by an

enteric layer which serves to resist disintegration in the stomach and permits the inner component to pass intact into the duodenum or to be delayed in release. A variety of materials can be used for such enteric layers or coatings, such materials including a number of polymeric acids with such materials as shellac, cetyl alcohol and cellulose acetate.

The liquid forms in which the novel compositions of the present invention may be advantageously incorporated for administration orally or by injection include aqueous solutions, suitably flavoured syrups, elixirs, aqueous or oil suspensions, and flavoured emulsions with edible oils such as cottonseed oil, sesame oil, coconut oil or peanut oil, as well as elixirs and similar pharmaceutical vehicles. Suitable dispersing or suspending agents for aqueous suspensions include synthetic and natural gums such as tragacanth, acacia, alginate, dextran, sodium carboxymethylcellulose, methylcellulose, polyvinylpyrrolidone or gelatin. The liquid forms are suitable in flavored suspending or dispersing agents such as the synthetic and natural gums, for example, tragacanth, acacia, methyl-cellulose and the like. Isotonic preparations which generally contain suitable preservatives are employed when intravenous administration is desired.

For liquid oral preparations, such as for example, suspensions, elixirs and solutions, suitable carriers and additives may advantageously include water, glycols, oils, alcohols, flavoring agents, preservatives, coloring agents and the like.

Forms useful for parenteral administration include sterile solutions, emulsions and suspensions. For parenterals, the carrier will usually comprise sterile water, through other ingredients, for example, for purposes such as aiding solubility or for preservation, may be included. Injectable suspensions may also be prepared, in which case appropriate liquid carriers, suspending agents and the like may be employed. For parenteral administration, sterile suspensions and solutions are desired. The pharmaceutical compositions herein will contain, per dosage unit, e.g. solution, suspension, emulsion, injection, teaspoonful and the like, an amount of the active ingredient necessary to deliver an effective dose as described above.

Depot formulations for intramuscular injection: Alternatively, the composition may be presented in a form suitable for once-weekly or once-monthly administration; for example, an insoluble salt of the active compound, such as the decanoate salt, may be adapted to provide a depot preparation for intramuscular injection.

Furthermore, compounds for the present invention can be administered in intranasal form via topical use of suitable intranasal vehicles, or via transdermal skin patches well known to those of ordinary skill in that art. To be administered in the form of transdermal delivery system, the dosage administration will, of course, be continuous rather than intermittent throughout the dosage regimen and dosage strength will need to be accordingly modified to obtain the desired therapeutic effects.

The compound of the present invention can also be administered in the form of liposome delivery systems, such as small unilamellar vesicles, large unilamellar vesicles, and multilamellar vesicles. Liposomes can be formed from a variety of phospholipids, such as cholesterol, stearylamine or phosphatidylcholines using processes well described in the art.

Compounds of this invention may be administered in any of the foregoing compositions and according to dosage regimens established in the art whenever treatment of the addressed disorders is required.

#### Dosis regimen and strength:

Advantageously, compounds of the present invention may be administered in a single daily dose, or the total daily dosage may be administered in divided doses of two, three or four times daily.

The daily dosage of the products may be varied over a wide range from 0.01 to 1.000 mg per adult human per day. For oral administration, the compositions are preferably provided in the form of tablets containing, 0.01, 0.05, 0.1, 0.5, 1.0, 2.5, 5.0, 10.0,

15.0, 25.0, 50.0, 100, 150, 200, 250, 500 and 1000 milligrams of the active ingredient for the symptomatic adjustment of the dosage to the patient to be treated. An effective amount of the drug is ordinarily supplied at a dosage level of from about 0.1 mg/kg to about 300 mg/kg of body weight per day. Preferably, the range is from about 1 to about 50 mg/kg of body weight per day. The compounds may be administered on a regimen of 1 to 4 times per day.

Optimal dosages to be administered may be readily determined by those skilled in the art, and will vary with the particular compound used, the mode of administration, the strength of the preparation, bioavailability due to the mode of administration, and the advancement of disease condition. In addition, factors associated with the particular patient being treated, including patient age, weight, diet and time of administration, should generally be considered in adjusting dosages.

The dosages, however, may be varied depending upon the requirement of the patients, the severity of the condition being treated and the compound being employed. The use of either daily administration or post-periodic dosing may be employed. Typically the dosage will be regulated by the physician based on the characteristics of the patient, his/her condition and the therapeutic effect desired.

The compounds or compositions of the present invention may be taken before a meal, while taking a meal or after a meal. When taken before a meal the compounds or composition of the present invention can be taken 1 hour, preferably 30 or even 15 or 5 minutes before eating. When taken while eating, the compounds or compositions of the present invention can be mixed into the meal or taken in a separate dosage form as described above. When taken after a meal, the compounds or compositions of the present invention can be taken 5, 15 or 30 minutes or even 1 hour after finishing a meal.

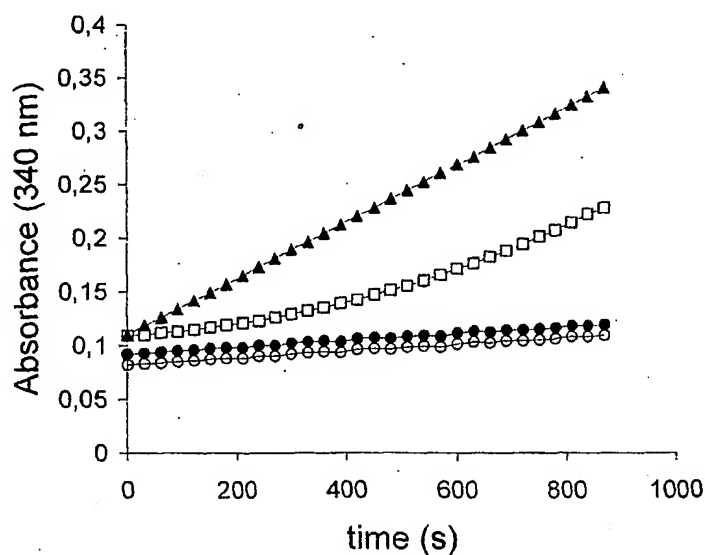
#### **Biochemistry: Inhibition constants for the DPIV inhibitors *in vitro* and *in vivo***

As indicated above, the compounds of the present invention and especially the compounds of the general formula (I), and their corresponding pharmaceutically

acceptable acid addition salt forms, are useful in inhibiting DPIV and DPIV – like enzyme activity. The ability of the compounds of the present invention, and their corresponding pharmaceutically acceptable acid addition salt forms to inhibit DPIV and DPIV – like enzyme activity may be demonstrated employing the DPIV activity assay for determination of the  $K_i$ -values *in vitro* and in human plasma.

The ability of the compounds of the present invention, and their corresponding pharmaceutically acceptable acid addition salt forms to inhibit DPIV *in vivo* may be demonstrated by oral or intravasal administration to Wistar rats. The compounds of the present invention inhibit DPIV activity *in vivo* after both, oral and intravasal administration to Wistar rats.

Further, the control of the half life period of the DPIV-Inhibitors *in vivo* by simultaneous administration of DP IV inhibitors and QC inhibitors can be demonstrated, as described in the following example



Assay:

All assays were performed at 30 °C using the Sunrise reader for microplates (TECAN). Assay mixtures contained the following constituents: 0.4 mM H-Gly-Pro-pNA, 0.65 mU DPIV in 0.04 M Hepes, pH 7.6, containing 0.104 M KCl (Figure 1, triangles). Additionally, samples contained either

- a)  $2.6 \cdot 10^{-5}$  M glutaminyl thiazolidine (open circles), or
- b)  $2.6 \cdot 10^{-5}$  M glutaminyl thiazolidine and 54 mU QC (squares) or
- c)  $2.6 \cdot 10^{-5}$  M glutaminyl thiazolidine, 54 mU QC and 0.4 mM 1-benzylimidazole (filled circles).

Reactions were started by addition of H-Gly-Pro-pNA when QC was omitted from the assay. Otherways, reactions were started by addition of a mixture of H-Gly-Pro-pNA and glutaminyl thiazolidine. Reactions were followed by monitoring the decrease in absorbance at 400 nm.

One unit of QC is defined as the amount of enzyme catalyzing the formation of 1  $\mu$ mol pGlu-pNA from H-Gln-pNA per minute at 30 °C in samples consisting of 0.2 mM fluorogenic substrate, 0.25 U pyroglutamyl aminopeptidase in 0.2 M Tris/HCl, pH 8.0 containing 20 mM EDTA. One unit of DPIV is defined as the amount of enzyme catalyzing the hydrolysis of 1  $\mu$ mol H-Gly-Pro-pNA per minute at 30 °C in samples consisting of 0.4 mM substrate in 0.04 M Hepes, pH 7.6 containing 0.104 M KCl.

As can be seen from the absorbance time diagram above, DPIV hydrolyzes H-Gly-Pro-pNA, which does not absorb at 340 nm (= H-glycyl-prolyl-para-nitroanilide) into H-Gly-Pro-OH and para-nitroaniline, which absorbs radiation of 340 nm; this reaction type is relatively fast and is represented by triangles.

If glutaminyl thiazolidine is added to the mixture of DP IV and H-Gly-Pro-pNA as in case (a), the reaction rate for the hydrolysis reaction decreases due to the competitive inhibition of DPIV by the DP IV inhibitor glutaminyl thiazolidine this reaction demonstrates the inhibitory action of glutaminyl thiazolidine in DP IV and is represented by open circles.

If, additionally in case (b), glutaminy cyclase is added the DP IV inhibitor glutaminy thiazolidine is degraded to the pyro-glutaminy-thiazolidine according to the reaction scheme mentioned above. The pyro-glutaminy-thiazolidine is formed by the cyclisation reaction of glutaminy thiazolidine through glutaminy cyclase (QC) according to the reaction scheme. The cyclic product, pyro-glutaminy-thiazolidine, is not active as an inhibitor for DP IV. Therefore the DP IV is only inhibited partially by glutaminy thiazolidine, which is reduced in its concentration by the simultaneously present glutaminy cyclase to the inactive cyclic pyro-derivate. Thus, the reaction rate for the hydrolysis reaction, represented by squares, is between the uninhibited reaction (triangles) and the strongly inhibited reaction (open circles, case (a)).

If, further additionally in case (c), benzimidazole is added to the reaction mixture, the reaction rate goes down as low as in case (a) where inhibition is only effected by the DP IV inhibitor glutaminy thiazolidine. This effect can be explained as follows: benzimidazole is an inhibitor of glutaminy cyclase which is therefore prevented to degrade the DP IV inhibitor glutaminy thiazolidine to the cyclic pyro-glutamine thiazolidine being inactive as a DP IV inhibitor.

Therefore, the concentration of the DP IV inhibitor glutaminy thiazolidine is maintained in the simultaneous presence of glutaminy cyclase (QC) and its inhibitor benzimidazole so as to glutaminy thiazolidine is capable of inhibiting DP IV to hydrolyse the chromogenic substrate H-Gly-Pro-pNA. Thus, the reaction rate for the hydrolysis reaction in case (c) marked with filled circles is as nearly as low as in case (a).

To summarize, it can be taken from the experiment above, that glutaminy thiazolidine is degraded to the cyclic pyro-glutamine derivate being inactive as a DP IV inhibitor. Thus, the half-life of glutaminy thiazolidine is reduced in the presence of QC (case (b)) resulting in a higher hydrolyses rate in the substrate compared with case (a) where no QC was present.



Further, it can be concluded from the above experiment that the half life of the DP IV inhibitor glutaminy l thiazolidine - in the presence of the enzyme glutaminy l cyclase , which is naturally present in humans -can be controlled by the addition of the glutaminy l cyclase inhibitor benzimidazole (case (c)). Thus, the hydrolysis reaction rate is decreased in case (c) compared with case (b), where no glutaminy l cyclase inhibitor such as benzimidazole was present.

Generally spoken, it means, that the addition of a QC inhibitor allows to control the half-life of action of a DP IV inhibitor according to the present invention to inhibit the DP IV enzyme by the mechanism described above. This is an essential aspect of this application.

DPIV is present in a wide variety of mammalian organs and tissues e.g. the intestinal brush-border (Gutschmidt S. et al., "In situ" - measurements of protein contents in the brush border region along rat jejunal villi and their correlations with four enzyme activities. *Histochemistry* 1981, 72 (3), 467-79), exocrine epithelia, hepatocytes, renal tubuli, endothelia, myofibroblasts (Feller A.C. et al., A monoclonal antibody detecting dipeptidylpeptidase IV in human tissue. *Virchows Arch. A. Pathol. Anat. Histopathol.* 1986; 409 (2):263-73), nerve cells, lateral membranes of certain surface epithelia, e.g. Fallopian tube, uterus and vesicular gland, in the luminal cytoplasm of e.g., vesicular gland epithelium, and in mucous cells of Brunner's gland (Hartel S. et al., Dipeptidyl peptidase (DPP) IV in rat organs. Comparison of immunohistochemistry and activity histochemistry. *Histochemistry* 1988; 89 (2): 151-61), reproductive organs, e.g. cauda epididymis and ampulla, seminal vesicles and their secretions (Agrawal & Vanha-Perttula, Dipeptidyl peptidases in bovine reproductive organs and secretions. *Int. J. Androl.* 1986, 9 (6): 435-52). In human serum, two molecular forms of dipeptidyl peptidase are present (Krepela E. et al., Demonstration of two molecular forms of dipeptidyl peptidase IV in normal human serum. *Physiol. Bohemoslov.* 1983, 32 (6): 486-96). The serum high molecular weight form of DPIV is expressed on the surface of activated T cells (Duke-Cohan J.S. et al., Serum high molecular weight dipeptidyl peptidase IV (CD26) is similar to a novel antigen DPPT-L released from activated T cells. *J. Immunol.* 1996, 156 (5): 1714-21).

The compounds of the present invention, and their corresponding pharmaceutically acceptable acid addition salt forms are able to inhibit DPIV *in vivo*. In one embodiment of the present invention, all molecular forms, homologues and epitopes of DPIV from all mammalian tissues and organs, also of those, which are undiscovered yet, are intended to be embraced by the scope of this invention.

Among the rare group of proline-specific proteases, DPIV was originally believed to be the only membrane-bound enzyme specific for proline as the penultimate residue at the amino-terminus of the polypeptide chain. However, other molecules, even structurally non-homologous with the DPIV but bearing corresponding enzyme activity, have been identified recently. DPIV-like enzymes, which are identified so far, are e.g. fibroblast activation protein  $\alpha$ , dipeptidyl peptidase IV  $\beta$ , dipeptidyl aminopeptidase-like protein, N-acetylated  $\alpha$ -linked acidic dipeptidase, quiescent cell proline dipeptidase, dipeptidyl peptidase II, attractin and dipeptidyl peptidase IV related protein (DPP 8), and are described in the review article by Sedo & Malik (Sedo & Malik, Dipeptidyl peptidase IV-like molecules: homologous proteins or homologous activities? *Biochimica et Biophysica Acta* 2001, 36506: 1-10).

Further DPIV-like enzymes are disclosed in WO 01/19866, WO 02/04610, WO 02/34900 and WO02/31134. WO 01/19866 discloses novel human dipeptidyl aminopeptidase (DPP8) with structural and functional similarities to DPIV and fibroblast activation protein (FAP). WO 02/04610 provides reagents, which regulate human dipeptidyl peptidase IV-like enzyme and reagents which bind to human dipeptidyl peptidase IV-like enzyme gene product. These reagents can play a role in preventing, ameliorating, or correcting dysfunctions or diseases including, but not limited to, tumors and peripheral and central nervous system disorders including pain and neurodegenerative disorders. The dipeptidyl peptidase IV-like enzyme of WO 02/04610 is well known in the art. In the Gene Bank data base, this enzyme is registered as KIAA1492 (registration in February 2001, submitted on April 04, 2000, AB040925).

WO 02/34900 discloses a dipeptidyl peptidase 9 (DPP9) with significant homology with the amino acid sequences of DPIV and DPP8. WO 02/31134 discloses three DPIV-like enzymes, DPRP1, DPRP2 and DPRP3. Sequence analysis revealed, that DPRP1 is identical to DPP8, as disclosed in WO 01/19866, that DPRP2 is identical to DPP9 and that DPRP3 is identical to KIAA1492 as disclosed in WO 02/04610.

In another preferred embodiment of the present invention, all molecular forms, homologues and epitopes of proteins comprising DPIV-like enzyme activity, from all mammalian tissues and organs, also of those, which are undiscovered yet, are intended to be embraced by the scope of this invention.

#### **In vivo Tests with diabetic Zucker rats**

The ability of the compounds of the present invention, and their corresponding pharmaceutically acceptable acid addition salt forms, to improve glucose tolerance in response to an oral glucose challenge, may be measured in diabetic Zucker rats. The method is described in examples 6 and 7. Oral administration of 5 mg/kg b.w., 15 mg/kg and 50 mg/kg b.w. of compounds according to the general formula (I) resulted in a dose dependent lowering of elevated blood glucose levels and thereby in an improvement of glucose tolerance in diabetic Zucker rats.

#### **Examples**

##### *Example 1 Synthesis of Boc-Gln(Trt)-Pro-NH<sub>2</sub>*

##### **Boc-Gln(Trt)-Pro-NH<sub>2</sub>**

Di-isopropylamine was added to a solution of H-ProNH<sub>2</sub>\*HCl in dry CH<sub>2</sub>Cl<sub>2</sub> until the pH was adjusted to 9. Boc-Gln(Trt)-OSu was added in one portion and the mixture stirred for 16h under an argon atmosphere. The solvent was evaporated and the residue treated in a standard way, i.e. the residue was partitioned between

ethylacetate and 0.3N KHSO<sub>4</sub> solution. The organic layer was further washed with saturated NaHCO<sub>3</sub> solution, water and brine. The solution was dried and evaporated at reduced pressure.

*Example 2 Synthesis of Boc-Gln(Trt)-Pyrr-CN*

**Boc-Gln(Trt)-Pyrr-CN**

Imidazole was added to a solution of Boc-Gln(Trt)-Pro-NH<sub>2</sub> in dry pyridine under an argon atmosphere. The solution was cooled to -35°C, before the dropwise addition of POCl<sub>3</sub>. The reaction was stirred at -30°C – to -20°C for 60min. The solution was then evaporated and the crude residue subjected to column chromatography (silica gel) to yield Boc-Gln(Trt)-Pyrr-CN of as a colourless oil.

*Example 3 Synthesis of H-Gln-Pyrr-CN\*TFA*

**H-Gln-Pyrr-CN\*TFA**

Deprotection was carried out by stirring with trifluoro acetic acid for 60min. Evaporation and lyophilisation from water afforded 2-(S)cyano-1-glutaminy pyrrolidine as a white solid.

*Example 4: K<sub>i</sub>-determination*

For K<sub>i</sub> determination of the compounds of the general formula (I), dipeptidyl peptidase IV from porcine kidney with a specific activity against glycylprolyl-4-nitroaniline of 37.5 U/mg and an enzyme concentration of 1.41 mg/ml in the stock solution was used.

**Assay mixture:**

100 µl of a solution containing the compound of the general formula (I) in a concentration range of 1\*10<sup>-5</sup> M – 1\*10<sup>-8</sup> M were admixed with 50 µl glycylprolyl-4-nitroaniline in different concentrations (0.4 mM, 0.2 mM, 0.1 mM, 0,05 mM) and

100  $\mu$ l HEPES (40 mM, pH7.6; ion strength = 0.125). The assay mixture was pre-incubated at 30 °C for 30 min. After pre-incubation, 20  $\mu$ l DPIV (1:600 diluted) were added and measurement of yellow color development due to 4-nitroaniline release was performed at 30°C and  $\lambda$  = 405 nm for 10 min using a plate reader (HTS7000 plus, Applied Biosystems, Weiterstadt, Germany).

The  $K_i$ -values were calculated using Graphit 4.0.15 (Erithacus Software, Ltd, UK) based on a competitive inhibition of DPIV by the compound of the general formula (I).

*Example 5:  $K_i$ -determination in human plasma*

Human plasma contains N-terminal Xaa-Pro releasing activity. (definition for Xaa: any amino acid, preferably an L- $\alpha$ -amino acid)

70  $\mu$ l of a solution of the compound of the general formula (I) in a concentration range of  $1 \cdot 10^{-5}$  M –  $1 \cdot 10^{-8}$  M were admixed with 50  $\mu$ l glycylprolyl-4-nitroaniline in different concentrations (0.4 mM, 0.2 mM, 0.1 mM, 0.05 mM) and 100  $\mu$ l HEPES (40 mM, pH 7.6). The assay mixture was pre-incubated at 30 °C for 5 min and 22 hours respectively. After pre-incubation, 50  $\mu$ l human plasma were added and measurement of yellow color development due to 4-nitroaniline release was performed at 30°C and  $\lambda$  = 405 nm for 10 min using a plate reader (HTS7000 plus, Applied Biosystems, Weiterstadt, Germany).

The  $K_i$ -values were calculated using Graphit 4.0.15 (Erithacus Software, Ltd, UK) based on a competitive inhibition of DPIV by the compound of the general formula (I).

*Example 6: Determination of DPIV inhibiting activity of a compound of the general formula (I) after intravasal and oral administration to Wistar rats*

### *Animals*

Male Wistar rats (Shoe: Wist(Sho)) with a body weight ranging between 250 and 350 g were purchased from Tierzucht Schönwalde (Schönwalde, Germany).

### *Housing conditions*

Animals were single-caged under conventional conditions with controlled temperature ( $22 \pm 2$  °C) on a 12/12 hours light/dark cycle (light on at 06:00 AM). Standard pelleted chow (ssniff® Soest, Germany) and tap water acidified with HCl were allowed ad libitum.

### *Catheter insertion into carotid artery*

After  $\geq$ one week of adaptation at the housing conditions, catheters were implanted into the carotid artery of Wistar rats under general anaesthesia (i.p. injection of 0.25 ml/kg b.w. Rompun® [2 %], BayerVital, Germany and 0.5 ml/kg b.w. Ketamin 10, Atarost GmbH & Co., Twistringen, Germany). The animals were allowed to recover for one week. The catheters were flushed with heparin-saline (100 IU/ml) three times per week.

In case of catheter dysfunction, a second catheter was inserted into the contra-lateral carotid artery of the respective rat. After one week of recovery from surgery, this animal was reintegrated into the study. In case of dysfunction of the second catheter, the animal was withdrawn from the study. A new animal was recruited and the experiments were continued in the planned sequence, beginning at least 7 days after catheter implantation.

### *Experimental design*

To rats with intact catheter function were administered placebo (1 ml saline, 0.154 mol/l) or 100 mg/kg b.w. of the compound of the general formula (I) via the oral and the intra-vascular (intra-arterial) route.

After overnight fasting, 100 µl samples of heparinised arterial blood were collected at -30, -5, and 0 min. The test substance was dissolved freshly in 1.0 ml saline (0.154 mol/l) and was administered at 0 min either orally via a feeding tube (75 mm; Fine Science Tools, Heidelberg, Germany) or via the intra-vascular route. In the case of oral

administration, an additional volume of 1 ml saline was injected into the arterial catheter. In the case of intra-arterial administration, the catheter was immediately flushed with 30  $\mu$ l saline and an additional 1 ml of saline was given orally via the feeding tube.

After application of placebo or the test substances, arterial blood samples were taken at 2.5, 5, 7.5, 10, 15, 20, 40, 60 and 120 min from the carotid catheter of the conscious unrestrained rats. All blood samples were collected into ice cooled Eppendorf tubes (Eppendorf-Netheler-Hinz, Hamburg, Germany) filled with 10  $\mu$ l 1M sodium citrate buffer (pH 3.0) for plasma DPIV activity measurement. Eppendorf tubes were centrifuged immediately (12000 rpm for 2 min, Hettich Zentrifuge EBA 12, Tuttlingen; Germany): The plasma fractions were stored on ice until analysis or were frozen at  $-20^{\circ}\text{C}$  until analysis. All plasma samples were labelled with the following data:

- Code number
- Animal Number
- Date of sampling
- Time of sampling

#### *Analytical Methods*

The assay mixture for determination of plasma DPIV activity consisted of 80  $\mu$ l reagent and 20  $\mu$ l plasma sample. Kinetic measurement of the formation of the yellow product 4-nitroaniline from the substrate glycylopropyl-4-nitroaniline was performed at 390 nm for 1 min at  $30^{\circ}\text{C}$  after 2 min pre-incubation at the same temperature. The DPIV activity was expressed in mU/ml.

#### *Statistical methods*

Statistical evaluations and graphics were performed with PRISM<sup>®</sup> 3.02 (GraphPad Software, Inc.). All parameters were analysed in a descriptive manner including mean and SD.

### *Results*

The compounds of the general formula (I) in a dose of 100 mg/kg b.w. vs. placebo inhibited plasma DPIV activity after oral and intra-vascular administration.

*Example 7: Dose escalation study in fatty Zucker rats after oral administration of a compound of the general formula (I)*

### *Animals*

N=30 male Zucker rats (fa/fa), mean age 11 weeks (5-12 weeks), mean body weight 350 g (150-400 g), were purchased from Charles River (Sulzfeld, Germany).

After delivery they were kept for >12 weeks until nearly all fatty Zucker rats had the characteristics of manifest diabetes mellitus. A group of N=8 animals were recruited for testing three escalating doses of a compound of the general formula (I) vs. placebo (saline).

### *Housing Conditions*

Animals were single-caged under standardized conditions with controlled temperature ( $22 \pm 2$  °C) on a 12/12 hours light/dark cycle (light on at 06:00 AM). Sterile standard pelleted chow (ssniff® Soest, Germany) and tap water acidified with HCl were allowed ad libitum.

### *Catheterization of Carotid Artery*

Fatty Zucker rats of 24-31 weeks (mean: 25 weeks) age, adapted to the housing conditions, were well prepared for the study.

Catheters were implanted into the carotid artery of fatty Zucker rats under general anaesthesia (i.p. injection of 0.25 ml/kg b.w. Rompun® [2 %], BayerVital, Germany and 0.5 ml/kg b.w. Ketamin 10, Atarost GmbH & Co., Twistringen, Germany). The animals were allowed to recover for one week. The catheters were flushed with heparin-saline (100 IU/ml) three times per week.



### *Experimental Design*

Placebo (1 ml saline, 0.154 mol/l) or escalating doses of a compound of the general formula (I) (5, 15 and 50 mg/kg b.w.) were administered to groups of N=8 fatty Zucker rats. 2 mmol of a compound of the general formula (I) were dissolved in 1000  $\mu$ l DMSO (E. Merck, Darmstadt; Germany [Dimethyl sulfoxide p.a.]). 10 ml saline were added and 1 ml aliquots, each containing 0,17 mmol of a compound of the general formula (I), were stored at  $-20^{\circ}\text{C}$ . For preparation of the test substance, dose dependent aliquots were diluted in saline.

After overnight fasting, placebo or test substance were administered to the fatty Zucker rats via feeding tube orally (15 G, 75 mm; Fine Science Tools, Heidelberg, Germany) at  $-10$  min. An oral glucose tolerance test (OGTT) with 2 g/kg b.w. glucose (40 % solution, B. Braun Melsungen, Melsungen, Germany) was administered at  $\pm 0$  min via a second feeding tube. Venous blood samples from the tail veins were collected at  $-30$  min,  $-15$  min,  $\pm 0$  min and at 5, 10, 15, 20, 30, 40, 60, 90 and 120 min into 20  $\mu$ l glass capillaries, which were placed in standard tubes filled with 1 ml solution for blood glucose measurement.

All blood samples were labelled with the following data:

- Code number
- Animal Number
- Date of sampling
- Time of sampling

### *Analytical Methods*

Glucose levels were measured using the glucose oxidase procedure (Super G Glucose analyzer; Dr. Müller Gerätebau, Freital, Germany).

### *Statistical methods*

Statistical evaluations and graphics were performed with PRISM<sup>®</sup> 3.02 (GraphPad Software, Inc.). All parameters were analysed in a descriptive manner including mean and SD.

*Effect of Medication on Glucose Tolerance*

The placebo treated diabetic Zucker rats showed a strongly elevated blood glucose excursion indicating glucose intolerance of manifest diabetes mellitus. Administration of 5 mg/kg b.w. of the compound of the general formula (I) resulted in a limited improvement of glucose tolerance in diabetic Zucker rats. Significant lowering of elevated blood glucose levels and improvement of glucose tolerance was achieved after administration of 15 mg/kg and 50 mg/kg b.w. of the compound according to general formula (I).

*Example 8: In vivo inactivation of a compound of the general formula (I) after oral administration to Wistar rats**Animals/Experimental design*

A compound of the general formula (I) was administered to Wistar rats orally as described in example 9. to determine the conversion to the corresponding cyclic inactive pyro-glutamine derivative compound.

*Analytical methods*

After application of placebo or a compound of the general formula (I), arterial blood samples were taken at 2.5, 5, 7.5, 10, 15, 20, 40, 60 and 120 min from the carotid catheter of the conscious unrestrained rats to determine the formation of degradation products of the compound of the general formula, the corresponding cyclic inactive pyro-glutamine derivative compound .

For analysis, simple solid phase extraction procedure on C18 cartridges was used to isolate the compounds of interest from the plasma. The extracts were analysed using reversed-phase liquid chromatography on Lichrospher 60 RP Select B column hyphenated with tandem mass spectrometry operating in the APCI positive mode. An internal standard method was used for quantification.

*Results*

After oral administration of a compound of the general formula (I) to Wistar rats, a degradation of the compound was found. Using LC/MS, the degradation product

could be indentified as the corresponding pyroglutaminyl derivative of the compound of the general formula (I).

#### *Example 9: Assays for glutaminyl cyclase activity*

##### *Fluorometric assays*

All measurements were performed with a BioAssay Reader HTS-7000Plus for microplates (Perkin Elmer) at 30 °C. QC activity was evaluated fluorometrically using H-Gln- $\beta$ NA. The samples consisted of 0.2 mM fluorogenic substrate, 0.25 U pyroglutamyl aminopeptidase (Unizyme, Hørsholm, Denmark) in 0.2 M Tris/HCl, pH 8.0 containing 20 mM EDTA and an appropriately diluted aliquot of QC in a final volume of 250  $\mu$ l. Excitation/emission wavelengths were 320/410 nm. The assay reactions were initiated by addition of glutaminyl cyclase. QC activity was determined from a standard curve of  $\beta$ -naphthylamine under assay conditions. One unit is defined as the amount of QC catalyzing the formation of 1  $\mu$ mol pGlu- $\beta$ NA from H-Gln- $\beta$ NA per minute under the described conditions.

In a second fluorometric assay, QC activity was determined using H-Gln-AMC as substrate. Reactions were carried out at 30°C utilizing the NOVOSTar reader for microplates (BMG labtechnologies). The samples consisted of varying concentrations of the fluorogenic substrate, 0.1 U pyroglutamyl aminopeptidase (Qiagen) in 0.05 M Tris/HCl, pH 8.0 containing 5 mM EDTA and an appropriately diluted aliquot of QC in a final volume of 250  $\mu$ l. Excitation/emission wavelengths were 380/460 nm. The assay reactions were initiated by addition of glutaminyl cyclase. QC activity was determined from a standard curve of 7-amino-4-methylcoumarin under assay conditions. The kinetic data were evaluated using GraFit software.

##### *Spectrophotometric assay of QC*

This novel assay was used to determine the kinetic parameters for most of the QC substrates. QC activity was analyzed spectrophotometrically using a continuous method, that was derived by adapting a previous discontinuous assay (Bateman, R. C. J. 1989 *J Neurosci Methods* 30, 23-28) utilizing glutamate dehydrogenase as

auxiliary enzyme. Samples consisted of the respective QC substrate, 0.3 mM NADH, 14 mM  $\alpha$ -Ketoglutaric acid and 30 U/ml glutamate dehydrogenase in a final volume of 250  $\mu$ l. Reactions were started by addition of QC and perused by monitoring of the decrease in absorbance at 340 nm for 8-15 min. Typical time courses of product formation are presented in Figure 1.

The initial velocities were evaluated and the enzymatic activity was determined from a standard curve of ammonia under assay conditions. All samples were measured at 30°C, using either the SPECTRAFluor Plus or the Sunrise (both from TECAN) reader for microplates. Kinetic data was evaluated using GraFit software.

#### *Inhibitor assay*

For inhibitor testing, the sample composition was the same as described above, except of the putative inhibitory compound added. For a rapid test of QC-inhibition, samples contained 4 mM of the respective inhibitor and a substrate concentration at 1  $K_M$ . For detailed investigations of the inhibition and determination of  $K_i$ -values, influence of the inhibitor on the auxiliary enzymes was investigated first. In every case, there was no influence on either enzyme detected, thus enabling the reliable determination of the QC inhibition. The inhibitory constant was evaluated by fitting the set of progress curves to the general equation for competitive inhibition using GraFit software.

## Claims

1. A compound of the general formula (I)



wherein n is 0 or 1;

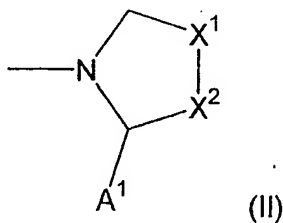
wherein  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ ,  $\text{R}^4$ ,  $\text{R}^5$ ,  $\text{R}^6$ ,  $\text{R}^7$ ,  $\text{R}^8$ ,  $\text{R}^9$ ,  $\text{R}^{10}$ , and  $\text{R}^{11}$ , independently of each other, are

- a hydrogen atom (-H), or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group or, a carbaldehyde (-CHO), a ketone group (-CO-R<sup>20</sup>), a boronic acid group (-B(OH)<sub>2</sub>), a cyano group (-C≡N), a carboxylic acid group (-COOH), a carboxylic acid ester group (-COOR<sup>21</sup>), a carboxylic acid anhydride group (-CO-O-CO-R<sup>22</sup>), a hydroxamic acid group (-CO-NH(OH)), a N-substituted hydroxamic acid group (-CO-NR<sup>23</sup>(OH)), a O-substituted hydroxamic acid group (-CO-NH(OR<sup>24</sup>)), a carboxamide group (-CO-NH<sub>2</sub>), a N-substituted or N,N-disubstituted carboxylic acid amide group, (-CO-NHR<sup>25</sup>, -CO-NR<sup>26</sup>R<sup>27</sup>), an amido group (-HN-CO-R<sup>28</sup>), a sulfonic acid group (-SO<sub>3</sub>H), a sulfonamide group (-SO<sub>2</sub>-NH<sub>2</sub>), a N-substituted or N,N-disubstituted sulfonamide group (-SO<sub>2</sub>-NHR<sup>29</sup>, -SO<sub>2</sub>-NR<sup>30</sup>R<sup>31</sup>), an amidosulfone group (-NH-SO<sub>2</sub>-R<sup>32</sup>), a sulfone group (-SO<sub>2</sub>-R<sup>33</sup>), a phosphoric acid group (-OP(=O)(OH)<sub>2</sub>), a phosphoric acid ester group (-OP(=O)(OR<sup>34</sup>)(OR<sup>35</sup>)), a phosphonic acid group (-P(=O)(OH)<sub>2</sub>), an phosphonic acid ester group (-P(=O)(OR<sup>36</sup>)(OR<sup>37</sup>)), a halogen atom, a trifluormethyl group (-CF<sub>3</sub>), a thiol group (-SH); a thioether group (-S-R<sup>38</sup>), a hydroxy group (-OH); an alkoxy group (-O-R<sup>39</sup>), a tetrazole group, an amino group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted amino group (-NHR<sup>40</sup>, -NR<sup>41</sup>R<sup>42</sup>);
- which each independently can be substituted with one or more substituents, which can be the same or different; and,

- wherein optionally, any **two of the groups**  $R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}$ , and  $R^{11}$ , as well the pairs  $R^{26}/R^{27}$ ,  $R^{30}/R^{31}$ ,  $R^{34}/R^{35}$ ,  $R^{36}/R^{37}$  and  $R^{41}/R^{42}$ , independently of each other, may form a part of a **ring**; and
- wherein the substituents  $R^{20}, R^{21}, R^{22}, R^{23}, R^{24}, R^{25}, R^{26}, R^{27}, R^{28}, R^{29}, R^{30}, R^{31}, R^{32}, R^{33}, R^{34}, R^{35}, R^{36}, R^{37}, R^{38}, R^{39}, R^{40}, R^{41}$ , and  $R^{42}$  independently of each other are a **hydrogen atom** (-H), or an **alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl** group; and
- wherein EWG1 and EWG2 are each independently an electron withdrawing group and;

wherein the group **PM**

has the formula (II)



- wherein  $X^1$  is  $CR^{51}R^{52}$ , O, S, SO, SO<sub>2</sub> or  $NR^{53}$ ; and
- wherein  $X^2$  is  $CR^{54}R^{55}$ , O, S, SO, SO<sub>2</sub>, or  $NR^{56}$ ; and

wherein  $R^{51}, R^{52}, R^{53}, R^{54}, R^{55}$ , and  $R^{56}$ , independently of each other, are

- a **hydrogen atom** (-H); or an **alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl,**

heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group or, a carbaldehyde (-CHO), a ketone group (-CO-R<sup>60</sup>), a boronic acid group (-B(OH)<sub>2</sub>), a cyano group (-C≡N), a carboxylic acid group (-COOH), a carboxylic acid ester group (-COOR<sup>61</sup>), a carboxylic acid anhydride group (-CO-O-CO-R<sup>62</sup>), a hydroxamic acid group (-CO-NH(OH)), a N-substituted hydroxamic acid group (-CO-NR<sup>63</sup>(OH)), a O-substituted hydroxamic acid group (-CO-NH(OR<sup>64</sup>)), a carboxamide group (-CO-NH<sub>2</sub>), a N-substituted or N,N-disubstituted carboxylic acid amide group, (-CO-NHR<sup>65</sup>; -CO-NR<sup>66</sup>R<sup>67</sup>), an amido group (-HN-CO-R<sup>68</sup>), a sulfonic acid group (-SO<sub>3</sub>H), a sulfonamide group (-SO<sub>2</sub>-NH<sub>2</sub>), a N-substituted or N,N-disubstituted sulfonamide group (-SO<sub>2</sub>-NHR<sup>69</sup>; -SO<sub>2</sub>-NR<sup>70</sup>R<sup>71</sup>), an amidosulfone group (-NH-SO<sub>2</sub>-R<sup>72</sup>), a sulfone group (-SO<sub>2</sub>-R<sup>73</sup>), a phosphoric acid group (-OP(=O)(OH)<sub>2</sub>), a phosphoric acid ester group (-OP(=O)(OR<sup>74</sup>)(OR<sup>75</sup>)), a phosphonic acid group (-P(=O)(OH)<sub>2</sub>), an phosphonic acid ester group (-P(=O)(OR<sup>76</sup>)(OR<sup>77</sup>)), a halogen atom, a trifluormethyl group (-CF<sub>3</sub>), a thiol group (-SH); a thioether group (-S-R<sup>78</sup>), a hydroxy group (-OH); an alkoxy group (-O-R<sup>79</sup>), a tetrazole group, an amino group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted amino group (-NHR<sup>80</sup>; -NR<sup>81</sup>R<sup>82</sup>); and

- which, independently of each other, can be substituted with one or more substituents, which can be the same or different; and,
- wherein optionally, any two of the groups R<sup>51</sup>, R<sup>52</sup>, R<sup>53</sup>, R<sup>54</sup>, R<sup>55</sup>, and R<sup>56</sup>, if present, as well as the pairs R<sup>66</sup>/R<sup>67</sup>, R<sup>70</sup>/R<sup>71</sup>, R<sup>74</sup>/R<sup>75</sup>, R<sup>76</sup>/R<sup>77</sup> and R<sup>81</sup>/R<sup>82</sup>, independently of each other, may form a part of a ring; and
- wherein the substituents R<sup>60</sup>, R<sup>61</sup>, R<sup>62</sup>, R<sup>63</sup>, R<sup>64</sup>, R<sup>65</sup>, R<sup>66</sup>, R<sup>67</sup>, R<sup>68</sup>, R<sup>69</sup>, R<sup>70</sup>, R<sup>71</sup>, R<sup>72</sup>, R<sup>73</sup>, R<sup>74</sup>, R<sup>75</sup>, R<sup>76</sup>, R<sup>77</sup>, R<sup>78</sup>, R<sup>79</sup>, R<sup>80</sup>, R<sup>81</sup>, and R<sup>82</sup>, independently of each other are a hydrogen atom (-H), or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl,

aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group; and

wherein A<sup>1</sup> is

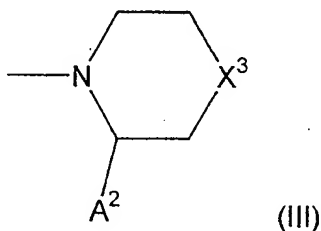
- a hydrogen atom (-H); or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group or, a carbaldehyde (-CHO), a ketone group (-CO-R<sup>100</sup>), a boronic acid group (-B(OH)<sub>2</sub>), a cyano group (-C≡N), a carboxylic acid group (-COOH), a carboxylic acid ester group (-COOR<sup>101</sup>), a carboxylic acid anhydride group (-CO-O-CO-R<sup>102</sup>), a hydroxamic acid group (-CO-NH(OH)), a N-substituted hydroxamic acid group (-CO-NR<sup>103</sup>(OH)), a O-substituted hydroxamic acid group (-CO-NH(OR<sup>104</sup>)), a carboxamide group (-CO-NH<sub>2</sub>), a N-substituted or N,N-disubstituted carboxylic acid amide group, (-CO-NHR<sup>105</sup>; -CO-NR<sup>106</sup>R<sup>107</sup>), an amido group (-HN-CO-R<sup>108</sup>), a sulfonic acid group (-SO<sub>3</sub>H), a sulfonamide group (-SO<sub>2</sub>-NH<sub>2</sub>), a N-substituted or N,N-disubstituted sulfonamide group (-SO<sub>2</sub>-NHR<sup>109</sup>; -SO<sub>2</sub>-NR<sup>110</sup>R<sup>111</sup>), an amidosulfone group (-NH-SO<sub>2</sub>-R<sup>112</sup>), a sulfone group (-SO<sub>2</sub>-R<sup>113</sup>), a phosphoric acid group (-OP(=O)(OH)<sub>2</sub>), a phosphoric acid ester group (-OP(=O)(OR<sup>114</sup>)(OR<sup>115</sup>)), a phosphonic acid group (-P(=O)(OH)<sub>2</sub>), an phosphonic acid ester group (-P(=O)(OR<sup>116</sup>)(OR<sup>117</sup>)), a halogen atom, a trifluormethyl group (-CF<sub>3</sub>), a thiol group (-SH); a thioether group (-S-R<sup>118</sup>), a hydroxy group (-OH); an alkoxy group (-O-R<sup>119</sup>), a tetrazole group, an amino group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted amino group (-NHR<sup>120</sup>; -NR<sup>121</sup>R<sup>122</sup>); and
- which, independently of each other, can be substituted with one or more substituents, which can be the same or different; and,
- wherein optionally, the pairs R<sup>106</sup>/R<sup>107</sup>, R<sup>110</sup>/R<sup>111</sup>, R<sup>114</sup>/R<sup>115</sup>, R<sup>116</sup>/R<sup>117</sup> and R<sup>121</sup>/R<sup>122</sup>, independently of each other, may form a part of a ring; and



- wherein the substituents  $R^{100}$ ,  $R^{101}$ ,  $R^{102}$ ,  $R^{103}$ ,  $R^{104}$ ,  $R^{105}$ ,  $R^{106}$ ,  $R^{107}$ ,  $R^{108}$ ,  $R^{109}$ ,  $R^{110}$ ,  $R^{111}$ ,  $R^{112}$ ,  $R^{113}$ ,  $R^{114}$ ,  $R^{115}$ ,  $R^{116}$ ,  $R^{117}$ ,  $R^{118}$ ,  $R^{119}$ ,  $R^{120}$ ,  $R^{121}$ , and  $R^{122}$ , independently of each other are a hydrogen atom (-H), or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group;

or wherein the group PM

has the formula (III)



- wherein  $X^3$  is  $CR^{131}R^{132}$ , O, S, SO, SO<sub>2</sub>, or  $NR^{133}$ ; and
- wherein  $R^{131}$ ,  $R^{132}$ , and  $R^{133}$ , independently of each other, are
- a hydrogen atom (-H); or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group or, a carbaldehyde (-CHO), a ketone group (-CO- $R^{140}$ ), a boronic acid group (-B(OH)<sub>2</sub>), a cyano group (-C≡N), a carboxylic acid group (-COOH), a carboxylic acid ester group (-COOR<sup>141</sup>), a carboxylic acid anhydride group (-CO-O-CO-R<sup>142</sup>), a hydroxamic acid group (-CO-NH(OH)), a N-substituted hydroxamic acid group (-CO-NR<sup>143</sup>(OH)), a O-substituted hydroxamic acid group (-CO-NH(OR<sup>144</sup>)), a carboxamide group (-CO-NH<sub>2</sub>), a N-substituted or N,N-disubstituted carboxylic acid amide group, (-CO-NHR<sup>145</sup>, -CO-NR<sup>146</sup>R<sup>147</sup>), an amido group (-HN-CO-R<sup>148</sup>), a sulfonic acid group (-SO<sub>3</sub>H), a sulfonamide group (-SO<sub>2</sub>-NH<sub>2</sub>), a N-substituted or N,N-

disubstituted **sulfonamide** group ( $-\text{SO}_2\text{-NHR}^{149}$ ;  $-\text{SO}_2\text{-NR}^{150}\text{R}^{151}$ ), an **amidosulfone** group ( $-\text{NH-SO}_2\text{-R}^{152}$ ), a **sulfone** group ( $-\text{SO}_2\text{-R}^{153}$ ), a **phosphoric acid** group ( $-\text{OP(=O)(OH)}_2$ ), a **phosphoric acid ester** group ( $-\text{OP(=O)(OR}^{154}\text{)(OR}^{155}\text{)}$ ), a **phosphonic acid** group ( $-\text{P(=O)(OH)}_2$ ), an **phosphonic acid ester** group ( $-\text{P(=O)(OR}^{156}\text{)(OR}^{157}\text{)}$ ), a **halogen atom**, a **trifluormethyl** group ( $-\text{CF}_3$ ), a **thiol** group ( $-\text{SH}$ ); a **thioether** group ( $-\text{S-R}^{158}$ ), a **hydroxy** group ( $-\text{OH}$ ); an **alkoxy** group ( $-\text{O-R}^{159}$ ), a **tetrazole** group, an **amino** group ( $-\text{NH}_2$ ), or a **N-substituted** or **N,N-disubstituted amino** group ( $-\text{NHR}^{160}$ ;  $-\text{NR}^{161}\text{R}^{162}$ ); and

- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; and,
- wherein optionally, the **the pair**  $\text{R}^{131}/\text{R}^{132}$ , if present, as well the pairs  $\text{R}^{146}/\text{R}^{147}$ ,  $\text{R}^{150}/\text{R}^{151}$ ,  $\text{R}^{154}/\text{R}^{155}$ ,  $\text{R}^{156}/\text{R}^{157}$  and  $\text{R}^{161}/\text{R}^{162}$ , independently of each other, may form a part of a ring; and
- wherein the substituents  $\text{R}^{140}$ ,  $\text{R}^{141}$ ,  $\text{R}^{142}$ ,  $\text{R}^{143}$ ,  $\text{R}^{144}$ ,  $\text{R}^{145}$ ,  $\text{R}^{146}$ ,  $\text{R}^{147}$ ,  $\text{R}^{148}$ ,  $\text{R}^{149}$ ,  $\text{R}^{150}$ ,  $\text{R}^{151}$ ,  $\text{R}^{152}$ ,  $\text{R}^{153}$ ,  $\text{R}^{154}$ ,  $\text{R}^{155}$ ,  $\text{R}^{156}$ ,  $\text{R}^{157}$ ,  $\text{R}^{158}$ ,  $\text{R}^{159}$ ,  $\text{R}^{160}$ ,  $\text{R}^{161}$ , and  $\text{R}^{162}$ , independently of each other are a **hydrogen atom** ( $-\text{H}$ ), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

wherein  $\text{A}^2$  is

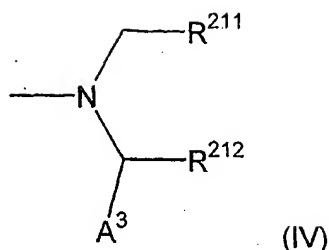
- a **hydrogen atom** ( $-\text{H}$ ); or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group or, a **carbaldehyde** ( $-\text{CHO}$ ), a **ketone** group ( $-\text{CO-R}^{180}$ ), a **boronic acid** group ( $-\text{B(OH)}_2$ ), a **cyano** group ( $-\text{C}\equiv\text{N}$ ), a **carboxylic acid** group ( $-\text{COOH}$ ), a **carboxylic acid ester** group ( $-\text{COOR}^{181}$ ), a

carboxylic acid anhydride group ( $-\text{CO}-\text{O}-\text{CO}-\text{R}^{182}$ ), a hydroxamic acid group ( $-\text{CO}-\text{NH}(\text{OH})$ ), a N-substituted hydroxamic acid group ( $-\text{CO}-\text{NR}^{183}(\text{OH})$ ), a O-substituted hydroxamic acid group ( $-\text{CO}-\text{NH}(\text{OR}^{184})$ ), a carboxamide group ( $-\text{CO}-\text{NH}_2$ ), a N-substituted or N,N-disubstituted carboxylic acid amide group, ( $-\text{CO}-\text{NHR}^{185}$ ;  $-\text{CO}-\text{NR}^{186}\text{R}^{187}$ ), an amido group ( $-\text{HN}-\text{CO}-\text{R}^{188}$ ), a sulfonic acid group ( $-\text{SO}_3\text{H}$ ), a sulfonamide group ( $-\text{SO}_2-\text{NH}_2$ ), a N-substituted or N,N-disubstituted sulfonamide group ( $-\text{SO}_2-\text{NHR}^{189}$ ;  $-\text{SO}_2-\text{NR}^{190}\text{R}^{191}$ ), an amidosulfone group ( $-\text{NH}-\text{SO}_2-\text{R}^{192}$ ), a sulfone group ( $-\text{SO}_2-\text{R}^{193}$ ), a phosphoric acid group ( $-\text{OP}(=\text{O})(\text{OH})_2$ ), a phosphoric acid ester group ( $-\text{OP}(=\text{O})(\text{OR}^{194})(\text{OR}^{195})$ ), a phosphonic acid group ( $-\text{P}(=\text{O})(\text{OH})_2$ ), an phosphonic acid ester group ( $-\text{P}(=\text{O})(\text{OR}^{196})(\text{OR}^{197})$ ), a halogen atom, a trifluormethyl group ( $-\text{CF}_3$ ), a thiol group ( $-\text{SH}$ ); a thioether group ( $-\text{S}-\text{R}^{198}$ ), a hydroxy group ( $-\text{OH}$ ); an alkoxy group ( $-\text{O}-\text{R}^{199}$ ), a tetrazole group, an amino group ( $-\text{NH}_2$ ), or a N-substituted or N,N-disubstituted amino group ( $-\text{NHR}^{200}$ ;  $-\text{NR}^{201}\text{R}^{202}$ ); and

- which, independently of each other, can be substituted with one or more substituents, which can be the same or different; and,
- wherein optionally, the pairs  $\text{R}^{186}/\text{R}^{187}$ ,  $\text{R}^{190}/\text{R}^{191}$ ,  $\text{R}^{194}/\text{R}^{195}$ ,  $\text{R}^{196}/\text{R}^{197}$  and  $\text{R}^{201}/\text{R}^{202}$  independently of each other, may form a part of a ring; and
- wherein the substituents  $\text{R}^{180}$ ,  $\text{R}^{181}$ ,  $\text{R}^{182}$ ,  $\text{R}^{183}$ ,  $\text{R}^{184}$ ,  $\text{R}^{185}$ ,  $\text{R}^{186}$ ,  $\text{R}^{187}$ ,  $\text{R}^{188}$ ,  $\text{R}^{189}$ ,  $\text{R}^{190}$ ,  $\text{R}^{191}$ ,  $\text{R}^{192}$ ,  $\text{R}^{193}$ ,  $\text{R}^{194}$ ,  $\text{R}^{195}$ ,  $\text{R}^{196}$ ,  $\text{R}^{197}$ ,  $\text{R}^{198}$ ,  $\text{R}^{199}$ ,  $\text{R}^{200}$ ,  $\text{R}^{201}$ , and  $\text{R}^{202}$ , independently of each other are a hydrogen atom ( $-\text{H}$ ), or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group;

or wherein the group PM

has the formula (IV)



- wherein  $R^{211}$  and  $R^{212}$ , independently of each other, are
- a hydrogen atom (-H); or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group or, a carbaldehyde (-CHO), a ketone group (-CO- $R^{220}$ ), a boronic acid group (-B(OH)<sub>2</sub>), a cyano group (-C≡N), a carboxylic acid group (-COOH), a carboxylic acid ester group (-COOR<sup>221</sup>), a carboxylic acid anhydride group (-CO-O-CO- $R^{222}$ ), a hydroxamic acid group (-CO-NH(OH)), a N-substituted hydroxamic acid group (-CO-NR<sup>223</sup>(OH)), a O-substituted hydroxamic acid group (-CO-NH(OR<sup>224</sup>)), a carboxamide group (-CO-NH<sub>2</sub>), a N-substituted or N,N-disubstituted carboxylic acid amide group, (-CO-NHR<sup>225</sup>; -CO-NR<sup>226</sup>R<sup>227</sup>), an amido group (-HN-CO- $R^{228}$ ), a sulfonic acid group (-SO<sub>3</sub>H), a sulfonamide group (-SO<sub>2</sub>-NH<sub>2</sub>), a N-substituted or N,N-disubstituted sulfonamide group (-SO<sub>2</sub>-NHR<sup>229</sup>; -SO<sub>2</sub>-NR<sup>230</sup>R<sup>231</sup>), an amidosulfone group (-NH-SO<sub>2</sub>- $R^{232}$ ), a sulfone group (-SO<sub>2</sub>- $R^{233}$ ), a phosphoric acid group (-OP(=O)(OH)<sub>2</sub>), a phosphoric acid ester group (-OP(=O)(OR<sup>234</sup>)(OR<sup>235</sup>)), a phosphonic acid group (-P(=O)(OH)<sub>2</sub>), an phosphonic acid ester group (-P(=O)(OR<sup>236</sup>)(OR<sup>237</sup>)), a halogen atom, a trifluormethyl group (-CF<sub>3</sub>), a thiol group (-SH); a thioether group (-S- $R^{238}$ ), a hydroxy group (-OH); an alkoxy group (-O- $R^{239}$ ), a tetrazole group, an amino group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted amino group (-NHR<sup>240</sup>; -NR<sup>241</sup>R<sup>242</sup>); and

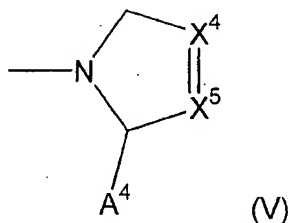
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; and,
- wherein optionally, the pairs  $R^{226}/R^{227}$ ,  $R^{230}/R^{231}$ ,  $R^{234}/R^{235}$ ,  $R^{236}/R^{237}$  and  $R^{241}/R^{242}$ , independently of each other, may form a part of a **ring**; and
  - wherein the substituents  $R^{220}$ ,  $R^{221}$ ,  $R^{222}$ ,  $R^{223}$ ,  $R^{224}$ ,  $R^{225}$ ,  $R^{226}$ ,  $R^{227}$ ,  $R^{228}$ ,  $R^{229}$ ,  $R^{230}$ ,  $R^{231}$ ,  $R^{232}$ ,  $R^{233}$ ,  $R^{234}$ ,  $R^{235}$ ,  $R^{236}$ ,  $R^{237}$ ,  $R^{238}$ ,  $R^{239}$ ,  $R^{240}$ ,  $R^{241}$ , and  $R^{242}$ , independently of each other are a **hydrogen atom (-H)**, or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;
- wherein  $A^3$  is
  - a **hydrogen atom (-H)**; or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group or, a **carbaldehyde (-CHO)**, a **ketone group (-CO-R<sup>260</sup>)**, a **boronic acid group (-B(OH)<sub>2</sub>)**, a **cyano group (-C≡N)**, a **carboxylic acid group (-COOH)**, a **carboxylic acid ester group (-COOR<sup>261</sup>)**, a **carboxylic acid anhydride group (-CO-O-CO-R<sup>262</sup>)**, a **hydroxamic acid group (-CO-NH(OH))**, a **N-substituted hydroxamic acid group (-CO-NR<sup>263</sup>(OH))**, a **O-substituted hydroxamic acid group (-CO-NH(OR<sup>264</sup>))**, a **carboxamide group (-CO-NH<sub>2</sub>)**, a **N-substituted or N,N-disubstituted carboxylic acid amide group, (-CO-NHR<sup>265</sup>; -CO-NR<sup>266</sup>R<sup>267</sup>)**, an **amido group (-HN-CO-R<sup>268</sup>)**, a **sulfonic acid group (-SO<sub>3</sub>H)**, a **sulfonamide group (-SO<sub>2</sub>-NH<sub>2</sub>)**, a **N-substituted or N,N-disubstituted sulfonamide group (-SO<sub>2</sub>-NHR<sup>269</sup>; -SO<sub>2</sub>-NR<sup>270</sup>R<sup>271</sup>)**, an **amidosulfone group (-NH-SO<sub>2</sub>-R<sup>272</sup>)**, a **sulfone group (-SO<sub>2</sub>-R<sup>273</sup>)**, a **phosphoric acid group (-OP(=O)(OH)<sub>2</sub>)**, a **phosphoric acid ester group (-OP(=O)(OR<sup>274</sup>)(OR<sup>275</sup>))**, a **phosphonic acid group (-P(=O)(OH)<sub>2</sub>)**, an

phosphonic acid ester group ( $-P(=O)(OR^{276})(OR^{277})$ ), a halogen atom, a trifluormethyl group ( $-CF_3$ ), a thiol group ( $-SH$ ); a thioether group ( $-S-R^{278}$ ), a hydroxy group ( $-OH$ ); an alkoxy group ( $-O-R^{279}$ ), a tetrazole group, an amino group ( $-NH_2$ ), or a N-substituted or N,N-disubstituted amino group ( $-NHR^{280}$ ,  $-NR^{281}R^{282}$ ); and

- which, independently of each other, can be substituted with one or more substituents, which can be the same or different; and,
- wherein optionally, the pairs  $R^{266}/R^{267}$ ,  $R^{270}/R^{271}$ ,  $R^{274}/R^{275}$ ,  $R^{276}/R^{277}$  and  $R^{281}/R^{282}$ , independently of each other, may form a part of a ring; and
- wherein the substituents  $R^{260}$ ,  $R^{261}$ ,  $R^{262}$ ,  $R^{263}$ ,  $R^{264}$ ,  $R^{265}$ ,  $R^{266}$ ,  $R^{267}$ ,  $R^{268}$ ,  $R^{269}$ ,  $R^{270}$ ,  $R^{271}$ ,  $R^{272}$ ,  $R^{273}$ ,  $R^{274}$ ,  $R^{275}$ ,  $R^{276}$ ,  $R^{277}$ ,  $R^{278}$ ,  $R^{279}$ ,  $R^{280}$ ,  $R^{281}$ , and  $R^{282}$ , independently of each other are a hydrogen atom ( $-H$ ), or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group;

or wherein the group PM

has the formula (V)



- wherein  $X^4$  is  $CR^{291}$  or N; and

- wherein  $X^5$  is  $CR^{292}$  or N; and
- wherein  $R^{291}$  and  $R^{292}$ , independently of each other, are
- a hydrogen atom (-H); or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group or, a carbaldehyde (-CHO), a ketone group ( $-CO-R^{300}$ ), a boronic acid group ( $-B(OH)_2$ ), a cyano group ( $-C\equiv N$ ), a carboxylic acid group ( $-COOH$ ), a carboxylic acid ester group ( $-COOR^{301}$ ), a carboxylic acid anhydride group ( $-CO-O-CO-R^{302}$ ), a hydroxamic acid group ( $-CO-NH(OH)$ ), a N-substituted hydroxamic acid group ( $-CO-NR^{303}(OH)$ ), a O-substituted hydroxamic acid group ( $-CO-NH(OR^{304})$ ), a carboxamide group ( $-CO-NH_2$ ), a N-substituted or N,N-disubstituted carboxylic acid amide group, ( $-CO-NHR^{305}$ ;  $-CO-NR^{306}R^{307}$ ), an amido group ( $-HN-CO-R^{308}$ ), a sulfonic acid group ( $-SO_3H$ ), a sulfonamide group ( $-SO_2-NH_2$ ), a N-substituted or N,N-disubstituted sulfonamide group ( $-SO_2-NHR^{309}$ ;  $-SO_2-NR^{310}R^{311}$ ), an amidosulfone group ( $-NH-SO_2-R^{312}$ ), a sulfone group ( $-SO_2-R^{313}$ ), a phosphoric acid group ( $-OP(=O)(OH)_2$ ), a phosphoric acid ester group ( $-OP(=O)(OR^{314})(OR^{315})$ ), a phosphonic acid group ( $-P(=O)(OH)_2$ ), an phosphonic acid ester group ( $-P(=O)(OR^{316})(OR^{317})$ ), a halogen atom, a trifluormethyl group ( $-CF_3$ ), a thiol group ( $-SH$ ); a thioether group ( $-S-R^{318}$ ), a hydroxy group ( $-OH$ ); an alkoxy group ( $-O-R^{319}$ ), a tetrazole group, an amino group ( $-NH_2$ ), or a N-substituted or N,N-disubstituted amino group ( $-NHR^{320}$ ;  $-NR^{321}R^{322}$ ); and
- which, independently of each other, can be substituted with one or more substituents, which can be the same or different; and,
- wherein optionally, the the pair  $R^{291}/R^{292}$ , if present, as well the pairs  $R^{306}/R^{307}$ ,  $R^{310}/R^{311}$ ,  $R^{314}/R^{315}$ ,  $R^{316}/R^{317}$  and  $R^{321}/R^{322}$ , independently of each other, may form a part of a ring; and

- wherein the substituents  $R^{300}$ ,  $R^{301}$ ,  $R^{302}$ ,  $R^{303}$ ,  $R^{304}$ ,  $R^{305}$ ,  $R^{306}$ ,  $R^{307}$ ,  $R^{308}$ ,  $R^{309}$ ,  $R^{310}$ ,  $R^{311}$ ,  $R^{312}$ ,  $R^{313}$ ,  $R^{314}$ ,  $R^{315}$ ,  $R^{316}$ ,  $R^{317}$ ,  $R^{318}$ ,  $R^{319}$ ,  $R^{320}$ ,  $R^{321}$ , and  $R^{322}$ , independently of each other are a hydrogen atom (-H), or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group;
- wherein  $A^4$  is
- a hydrogen atom (-H); or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group or, a carbaldehyde (-CHO), a ketone group ( $-\text{CO}-R^{340}$ ), a boronic acid group ( $-\text{B}(\text{OH})_2$ ), a cyano group ( $-\text{C}\equiv\text{N}$ ), a carboxylic acid group ( $-\text{COOH}$ ), a carboxylic acid ester group ( $-\text{COOR}^{341}$ ), a carboxylic acid anhydride group ( $-\text{CO}-\text{O}-\text{CO}-R^{342}$ ), a hydroxamic acid group ( $-\text{CO}-\text{NH}(\text{OH})$ ), a N-substituted hydroxamic acid group ( $-\text{CO}-\text{NR}^{343}(\text{OH})$ ), a O-substituted hydroxamic acid group ( $-\text{CO}-\text{NH}(\text{OR}^{344})$ ), a carboxamide group ( $-\text{CO}-\text{NH}_2$ ), a N-substituted or N,N-disubstituted carboxylic acid amide group, ( $-\text{CO}-\text{NHR}^{345}$ ,  $-\text{CO}-\text{NR}^{346}\text{R}^{347}$ ), an amido group ( $-\text{HN}-\text{CO}-\text{R}^{348}$ ), a sulfonic acid group ( $-\text{SO}_3\text{H}$ ), a sulfonamide group ( $-\text{SO}_2-\text{NH}_2$ ), a N-substituted or N,N-disubstituted sulfonamide group ( $-\text{SO}_2-\text{NHR}^{349}$ ,  $-\text{SO}_2-\text{NR}^{350}\text{R}^{351}$ ), an amidosulfone group ( $-\text{NH}-\text{SO}_2-\text{R}^{352}$ ), a sulfone group ( $-\text{SO}_2-\text{R}^{353}$ ), a phosphoric acid group ( $-\text{OP}(=\text{O})(\text{OH})_2$ ), a phosphoric acid ester group ( $-\text{OP}(=\text{O})(\text{OR}^{354})(\text{OR}^{355})$ ), a phosphonic acid group ( $-\text{P}(=\text{O})(\text{OH})_2$ ), an phosphonic acid ester group ( $-\text{P}(=\text{O})(\text{OR}^{356})(\text{OR}^{357})$ ), a halogen atom, a trifluormethyl group ( $-\text{CF}_3$ ), a thiol group ( $-\text{SH}$ ); a thioether group ( $-\text{S}-\text{R}^{358}$ ), a hydroxy group ( $-\text{OH}$ ); an alkoxy group ( $-\text{O}-\text{R}^{359}$ ), a tetrazole group, an amino group ( $-\text{NH}_2$ ), or a N-substituted or N,N-disubstituted amino group ( $-\text{NHR}^{360}$ ,  $-\text{NR}^{361}\text{R}^{362}$ ); and

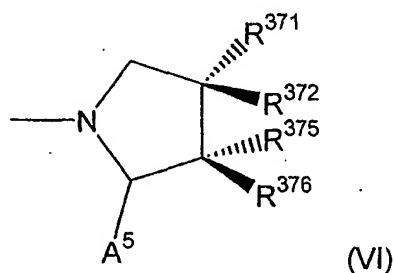


354

- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the pairs  $R^{346}/R^{347}$ ,  $R^{350}/R^{351}$ ,  $R^{354}/R^{355}$ ,  $R^{356}/R^{357}$  and  $R^{361}/R^{362}$ , independently of each other, may form a part of a **ring**; and
- wherein the substituents  $R^{340}$ ,  $R^{341}$ ,  $R^{342}$ ,  $R^{343}$ ,  $R^{344}$ ,  $R^{345}$ ,  $R^{346}$ ,  $R^{347}$ ,  $R^{348}$ ,  $R^{349}$ ,  $R^{350}$ ,  $R^{351}$ ,  $R^{352}$ ,  $R^{353}$ ,  $R^{354}$ ,  $R^{355}$ ,  $R^{356}$ ,  $R^{357}$ ,  $R^{358}$ ,  $R^{359}$ ,  $R^{360}$ ,  $R^{361}$ , and  $R^{362}$ , independently of each other are a **hydrogen atom (-H)**, or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

or wherein the group **PM**

has the formula (VI)



- wherein  $R^{371}$ ,  $R^{372}$ ,  $R^{375}$  and  $R^{376}$ , independently of each other, a **hydrogen atom (-H)**; or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group or, a **carbaldehyde (-CHO)**, a

ketone group ( $-\text{CO}-\text{R}^{380}$ ), a boronic acid group ( $-\text{B}(\text{OH})_2$ ), a cyano group ( $-\text{C}\equiv\text{N}$ ), a carboxylic acid group ( $-\text{COOH}$ ), a carboxylic acid ester group ( $-\text{COOR}^{381}$ ), a carboxylic acid anhydride group ( $-\text{CO}-\text{O}-\text{CO}-\text{R}^{382}$ ), a hydroxamic acid group ( $-\text{CO}-\text{NH}(\text{OH})$ ), a N-substituted hydroxamic acid group ( $-\text{CO}-\text{NR}^{383}(\text{OH})$ ), a O-substituted hydroxamic acid group ( $-\text{CO}-\text{NH}(\text{OR}^{384})$ ), a carboxamide group ( $-\text{CO}-\text{NH}_2$ ), a N-substituted or N,N-disubstituted carboxylic acid amide group, ( $-\text{CO}-\text{NHR}^{385}$ ;  $-\text{CO}-\text{NR}^{386}\text{R}^{387}$ ), an amido group ( $-\text{HN}-\text{CO}-\text{R}^{388}$ ), a sulfonic acid group ( $-\text{SO}_3\text{H}$ ), a sulfonamide group ( $-\text{SO}_2-\text{NH}_2$ ), a N-substituted or N,N-disubstituted sulfonamide group ( $-\text{SO}_2-\text{NHR}^{389}$ ;  $-\text{SO}_2-\text{NR}^{390}\text{R}^{391}$ ), an amidosulfone group ( $-\text{NH}-\text{SO}_2-\text{R}^{392}$ ), a sulfone group ( $-\text{SO}_2-\text{R}^{393}$ ), a phosphoric acid group ( $-\text{OP}(=\text{O})(\text{OH})_2$ ), a phosphoric acid ester group ( $-\text{OP}(=\text{O})(\text{OR}^{394})(\text{OR}^{395})$ ), a phosphonic acid group ( $-\text{P}(=\text{O})(\text{OH})_2$ ), an phosphonic acid ester group ( $-\text{P}(=\text{O})(\text{OR}^{396})(\text{OR}^{397})$ ), a halogen atom, a trifluormethyl group ( $-\text{CF}_3$ ), a thiol group ( $-\text{SH}$ ); a thioether group ( $-\text{S}-\text{R}^{398}$ ), a hydroxy group ( $-\text{OH}$ ); an alkoxy group ( $-\text{O}-\text{R}^{399}$ ), a tetrazole group, an amino group ( $-\text{NH}_2$ ), or a N-substituted or N,N-disubstituted amino group ( $-\text{NHR}^{400}$ ;  $-\text{NR}^{401}\text{R}^{402}$ ); and

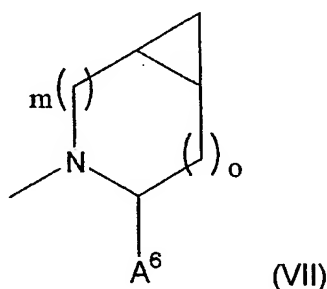
- which, independently of each other, can be substituted with one or more substituents, which can be the same or different; and,
- wherein optionally, any two of the groups  $\text{R}^{371}$ ,  $\text{R}^{372}$ ,  $\text{R}^{375}$ , and  $\text{R}^{376}$ , as well as the pairs  $\text{R}^{386}/\text{R}^{387}$ ,  $\text{R}^{390}/\text{R}^{391}$ ,  $\text{R}^{394}/\text{R}^{395}$ ,  $\text{R}^{396}/\text{R}^{397}$  and  $\text{R}^{401}/\text{R}^{402}$ , independently of each other, may form a part of a ring; and
- wherein the substituents  $\text{R}^{380}$ ,  $\text{R}^{381}$ ,  $\text{R}^{382}$ ,  $\text{R}^{383}$ ,  $\text{R}^{384}$ ,  $\text{R}^{385}$ ,  $\text{R}^{386}$ ,  $\text{R}^{387}$ ,  $\text{R}^{388}$ ,  $\text{R}^{389}$ ,  $\text{R}^{390}$ ,  $\text{R}^{391}$ ,  $\text{R}^{392}$ ,  $\text{R}^{393}$ ,  $\text{R}^{394}$ ,  $\text{R}^{395}$ ,  $\text{R}^{396}$ ,  $\text{R}^{397}$ ,  $\text{R}^{398}$ ,  $\text{R}^{399}$ ,  $\text{R}^{400}$ ,  $\text{R}^{401}$ , and  $\text{R}^{402}$ , independently of each other are a hydrogen atom ( $-\text{H}$ ), or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group; or

- alternatively; the two groups  $R^{371}$  and  $R^{372}$  can be together an **oxo** ( $=O$ ) or **hydroxyimino** ( $=N-OH$ ) group; and
- alternatively; the two groups  $R^{375}$  and  $R^{376}$  can be together an **oxo** ( $=O$ ) or **hydroxyimino** ( $=N-OH$ ) group; and
- 
- wherein  $A^5$  is
- a **hydrogen** atom ( $-H$ ); or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group or, a **carbaldehyde** ( $-CHO$ ), a **ketone** group ( $-CO-R^{420}$ ), a **boronic acid** group ( $-B(OH)_2$ ), a **cyano** group ( $-C\equiv N$ ), a **carboxylic acid** group ( $-COOH$ ), a **carboxylic acid ester** group ( $-COOR^{421}$ ), a **carboxylic acid anhydride** group ( $-CO-O-CO-R^{422}$ ), a **hydroxamic acid** group ( $-CO-NH(OH)$ ), a **N-substituted hydroxamic acid** group ( $-CO-NR^{423}(OH)$ ), a **O-substituted hydroxamic acid** group ( $-CO-NH(OR^{424})$ ), a **carboxamide** group ( $-CO-NH_2$ ), a **N-substituted or N,N-disubstituted carboxylic acid amide** group, ( $-CO-NHR^{425}$ ;  $-CO-NR^{426}R^{427}$ ), an **amido** group ( $-HN-CO-R^{428}$ ), a **sulfonic acid** group ( $-SO_3H$ ), a **sulfonamide** group ( $-SO_2-NH_2$ ), a **N-substituted or N,N-disubstituted sulfonamide** group ( $-SO_2-NHR^{429}$ ;  $-SO_2-NR^{430}R^{431}$ ), an **amidosulfone** group ( $-NH-SO_2-R^{432}$ ), a **sulfone** group ( $-SO_2-R^{433}$ ), a **phosphoric acid** group ( $-OP(=O)(OH)_2$ ), a **phosphoric acid ester** group ( $-OP(=O)(OR^{434})(OR^{435})$ ), a **phosphonic acid** group ( $-P(=O)(OH)_2$ ), an **phosphonic acid ester** group ( $-P(=O)(OR^{436})(OR^{437})$ ), a **halogen atom**, a **trifluormethyl** group ( $-CF_3$ ), a **thiol** group ( $-SH$ ); a **thioether** group ( $-S-R^{438}$ ), a **hydroxy** group ( $-OH$ ); an **alkoxy** group ( $-O-R^{439}$ ), a **tetrazole** group, an **amino** group ( $-NH_2$ ), or a **N-substituted or N,N-disubstituted amino** group ( $-NHR^{440}$ ;  $-NR^{441}R^{442}$ ); and
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; and,

- wherein optionally, the pairs  $R^{426}/R^{427}$ ,  $R^{430}/R^{431}$ ,  $R^{434}/R^{435}$ ,  $R^{436}/R^{437}$  and  $R^{441}/R^{442}$ , independently of each other, may form a part of a **ring**; and
- wherein the substituents  $R^{420}$ ,  $R^{421}$ ,  $R^{422}$ ,  $R^{423}$ ,  $R^{424}$ ,  $R^{425}$ ,  $R^{426}$ ,  $R^{427}$ ,  $R^{428}$ ,  $R^{429}$ ,  $R^{430}$ ,  $R^{431}$ ,  $R^{432}$ ,  $R^{433}$ ,  $R^{434}$ ,  $R^{435}$ ,  $R^{436}$ ,  $R^{437}$ ,  $R^{438}$ ,  $R^{439}$ ,  $R^{440}$ ,  $R^{441}$ , and  $R^{442}$ , independently of each other are a **hydrogen atom (-H)**, or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

or wherein the group **PM**

has the formula (VII)

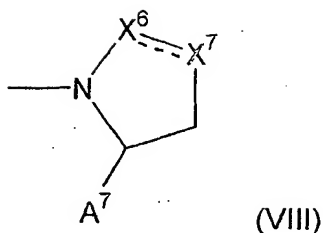


- wherein  $m$  is equal to 1 or 2, and  $o$  is equal to 1 or 2, and  $m$  or  $o$  can be 0;
- wherein  $A^6$  is a **hydrogen atom (-H)**; or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group or, a **carbaldehyde** (-CHO), a **ketone group** (-CO- $R^{460}$ ), a **boronic acid group** (-B(OH)<sub>2</sub>), a **cyano group** (-C≡N), a **carboxylic acid group** (-COOH), a **carboxylic acid ester group**

- (-COOR<sup>461</sup>), a **carboxylic acid anhydride** group (-CO-O-CO-R<sup>462</sup>), a **hydroxamic acid** group (-CO-NH(OH)), a N-substituted **hydroxamic acid** group (-CO-NR<sup>463</sup>(OH)), a O-substituted **hydroxamic acid** group (-CO-NH(OR<sup>464</sup>)), a **carboxamide** group (-CO-NH<sub>2</sub>), a N-substituted or N,N-disubstituted **carboxylic acid amide** group, (-CO-NHR<sup>465</sup>; -CO-NR<sup>466</sup>R<sup>467</sup>), an **amido** group (-HN-CO-R<sup>468</sup>), a **sulfonic acid** group (-SO<sub>3</sub>H), a **sulfonamide** group (-SO<sub>2</sub>-NH<sub>2</sub>), a N-substituted or N,N-disubstituted **sulfonamide** group (-SO<sub>2</sub>-NHR<sup>469</sup>; -SO<sub>2</sub>-NR<sup>470</sup>R<sup>471</sup>), an **amidosulfone** group (-NH-SO<sub>2</sub>-R<sup>472</sup>), a **sulfone** group (-SO<sub>2</sub>-R<sup>473</sup>), a **phosphoric acid** group (-OP(=O)(OH)<sub>2</sub>), a **phosphoric acid ester** group (-OP(=O)(OR<sup>474</sup>)(OR<sup>475</sup>)), a **phosphonic acid** group (-P(=O)(OH)<sub>2</sub>), an **phosphonic acid ester** group (-P(=O)(OR<sup>476</sup>)(OR<sup>477</sup>)), a **halogen atom**, a **trifluormethyl** group (-CF<sub>3</sub>), a **thiol** group (-SH); a **thioether** group (-S-R<sup>478</sup>), a **hydroxy** group (-OH); an **alkoxy** group (-O-R<sup>479</sup>), a **tetrazole** group, an **amino** group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted **amino** group (-NHR<sup>480</sup>; -NR<sup>481</sup>R<sup>482</sup>);
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; and,
  - wherein optionally, the pairs R<sup>466</sup>/R<sup>467</sup>, R<sup>470</sup>/R<sup>471</sup>, R<sup>474</sup>/R<sup>475</sup>, R<sup>476</sup>/R<sup>477</sup> and R<sup>481</sup>/R<sup>482</sup>, independently of each other, may form a part of a **ring**; and
  - wherein the substituents R<sup>460</sup>, R<sup>461</sup>, R<sup>462</sup>, R<sup>463</sup>, R<sup>464</sup>, R<sup>465</sup>, R<sup>466</sup>, R<sup>467</sup>, R<sup>468</sup>, R<sup>469</sup>, R<sup>470</sup>, R<sup>471</sup>, R<sup>472</sup>, R<sup>473</sup>, R<sup>474</sup>, R<sup>475</sup>, R<sup>476</sup>, R<sup>477</sup>, R<sup>478</sup>, R<sup>479</sup>, R<sup>480</sup>, R<sup>481</sup>, and R<sup>482</sup>, independently of each other are a **hydrogen atom**, (-H), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

or wherein the group **PM**

has the formula (VIII)



- wherein  $X^6$  is selected from  $CR^{490}R^{491}$ , O, S or  $NR^{492}$ , when the bond between  $X^6$  and  $X^7$  is a single bond; and
- wherein  $X^7$  is selected from  $CR^{493}R^{494}$ , O, S, or  $NR^{495}$ , when the bond between  $X^6$  and  $X^7$  is a single bond;
- **or alternatively,**
- wherein  $X^6$  is selected from  $CR^{496}$  or N, when the bond between  $X^6$  and  $X^7$  is a double bond; and
- wherein  $X^7$  is selected from  $CR^{497}$  or N, when the bond between  $X^6$  and  $X^7$  is a double bond; and
- wherein  $R^{490}$ ,  $R^{491}$ ,  $R^{492}$ ,  $R^{493}$ ,  $R^{494}$ ,  $R^{495}$ ,  $R^{496}$ , and  $R^{497}$ , independently of each other, are a **hydrogen atom (-H)**; or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group or, a **carbaldehyde** (-CHO), a **ketone** group (-CO- $R^{500}$ ), a **boronic acid** group (-B(OH)<sub>2</sub>), a **cyano** group (-C≡N), a **carboxylic acid** group (-COOH), a **carboxylic acid ester** group (-COOR<sup>501</sup>), a **carboxylic acid anhydride** group (-CO-O-CO-R<sup>502</sup>), a **hydroxamic acid** group (-CO-NH(OH)), a **N-substituted hydroxamic acid** group (-CO-NR<sup>503</sup>(OH)), a **O-substituted hydroxamic acid** group (-CO-NH(OR<sup>504</sup>)), a **carboxamide** group (-CO-NH<sub>2</sub>), a **N-substituted or N,N-disubstituted carboxylic acid amide** group, (-CO-NHR<sup>505</sup>, -CO-NR<sup>506</sup>R<sup>507</sup>), an **amido** group (-HN-CO-

$R^{508}$ ), a **sulfonic acid** group ( $-\text{SO}_3\text{H}$ ), a **sulfonamide** group ( $-\text{SO}_2-\text{NH}_2$ ), a **N-substituted** or **N,N-disubstituted sulfonamide** group ( $-\text{SO}_2-\text{NHR}^{509}$ ,  $-\text{SO}_2-\text{NR}^{510}\text{R}^{511}$ ), an **amidosulfone** group ( $-\text{NH}-\text{SO}_2-\text{R}^{512}$ ), a **sulfone** group ( $-\text{SO}_2-\text{R}^{513}$ ), a **phosphoric acid** group ( $-\text{OP}(=\text{O})(\text{OH})_2$ ), a **phosphoric acid ester** group ( $-\text{OP}(=\text{O})(\text{OR}^{514})(\text{OR}^{515})$ ), a **phosphonic acid** group ( $-\text{P}(=\text{O})(\text{OH})_2$ ), an **phosphonic acid ester** group ( $-\text{P}(=\text{O})(\text{OR}^{516})(\text{OR}^{517})$ ), a **halogen atom**, a **trifluormethyl** group ( $-\text{CF}_3$ ), a **thiol** group ( $-\text{SH}$ ), a **thioether** group ( $-\text{S}-\text{R}^{518}$ ), a **hydroxy** group ( $-\text{OH}$ ), an **alkoxy** group ( $-\text{O}-\text{R}^{519}$ ), a **tetrazole** group, an **amino** group ( $-\text{NH}_2$ ), or a **N-substituted** or **N,N-disubstituted amino** group ( $-\text{NHR}^{520}$ ,  $-\text{NR}^{521}\text{R}^{522}$ ); and

- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, any two the groups  $R^{490}$ ,  $R^{491}$ ,  $R^{492}$ ,  $R^{493}$ ,  $R^{494}$ ,  $R^{495}$ ,  $R^{496}$ , and  $R^{497}$ , if present, as well as the pairs  $R^{506}/R^{507}$ ,  $R^{510}/R^{511}$ ,  $R^{514}/R^{515}$ ,  $R^{516}/R^{517}$  and  $R^{521}/R^{522}$ , independently of each other, may form a part of a **ring**; and
- wherein the substituents  $R^{500}$ ,  $R^{501}$ ,  $R^{502}$ ,  $R^{503}$ ,  $R^{504}$ ,  $R^{505}$ ,  $R^{506}$ ,  $R^{507}$ ,  $R^{508}$ ,  $R^{509}$ ,  $R^{510}$ ,  $R^{511}$ ,  $R^{512}$ ,  $R^{513}$ ,  $R^{514}$ ,  $R^{515}$ ,  $R^{516}$ ,  $R^{517}$ ,  $R^{518}$ ,  $R^{519}$ ,  $R^{520}$ ,  $R^{521}$ , and  $R^{522}$ , independently of each other are a **hydrogen atom** ( $-\text{H}$ ), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group; and
- wherein  $A^7$  is
- a **hydrogen atom** ( $-\text{H}$ ); or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group or, a **carbaldehyde** ( $-\text{CHO}$ ), a **ketone** group ( $-\text{CO}-\text{R}^{540}$ ), a **boronic acid** group ( $-\text{B}(\text{OH})_2$ ), a **cyano** group ( $-\text{C}\equiv\text{N}$ ), a **carboxylic acid** group ( $-\text{COOH}$ ), a **carboxylic acid ester** group ( $-\text{COOR}^{541}$ ), a

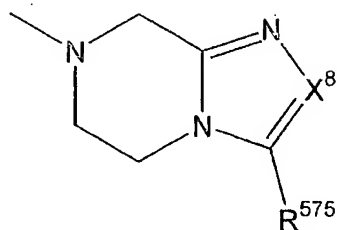
carboxylic acid anhydride group ( $-\text{CO}-\text{O}-\text{CO}-\text{R}^{542}$ ), a hydroxamic acid group ( $-\text{CO}-\text{NH}(\text{OH})$ ), a N-substituted hydroxamic acid group ( $-\text{CO}-\text{NR}^{543}(\text{OH})$ ), a O-substituted hydroxamic acid group ( $-\text{CO}-\text{NH}(\text{OR}^{544})$ ), a carboxamide group ( $-\text{CO}-\text{NH}_2$ ), a N-substituted or N,N-disubstituted carboxylic acid amide group, ( $-\text{CO}-\text{NHR}^{545}$ ;  $-\text{CO}-\text{NR}^{546}\text{R}^{547}$ ), an amido group ( $-\text{HN}-\text{CO}-\text{R}^{548}$ ), a sulfonic acid group ( $-\text{SO}_3\text{H}$ ), a sulfonamide group ( $-\text{SO}_2-\text{NH}_2$ ), a N-substituted or N,N-disubstituted sulfonamide group ( $-\text{SO}_2-\text{NHR}^{549}$ ;  $-\text{SO}_2-\text{NR}^{550}\text{R}^{551}$ ), an amidosulfone group ( $-\text{NH}-\text{SO}_2-\text{R}^{552}$ ), a sulfone group ( $-\text{SO}_2-\text{R}^{553}$ ), a phosphoric acid group ( $-\text{OP}(=\text{O})(\text{OH})_2$ ), a phosphoric acid ester group ( $-\text{OP}(=\text{O})(\text{OR}^{554})(\text{OR}^{555})$ ), a phosphonic acid group ( $-\text{P}(=\text{O})(\text{OH})_2$ ), an phosphonic acid ester group ( $-\text{P}(=\text{O})(\text{OR}^{556})(\text{OR}^{557})$ ), a halogen atom, a trifluormethyl group ( $-\text{CF}_3$ ), a thiol group ( $-\text{SH}$ ), a thioether group ( $-\text{S}-\text{R}^{558}$ ), a hydroxy group ( $-\text{OH}$ ), an alkoxy group ( $-\text{O}-\text{R}^{559}$ ), a tetrazole group, an amino group ( $-\text{NH}_2$ ), or a N-substituted or N,N-disubstituted amino group ( $-\text{NHR}^{560}$ ;  $-\text{NR}^{561}\text{R}^{562}$ ); and

- which, independently of each other, can be substituted with one or more substituents, which can be the same or different; and,
- wherein optionally, the pairs  $\text{R}^{546}/\text{R}^{547}$ ,  $\text{R}^{550}/\text{R}^{551}$ ,  $\text{R}^{554}/\text{R}^{555}$ ,  $\text{R}^{556}/\text{R}^{557}$  and  $\text{R}^{561}/\text{R}^{562}$ , independently of each other, may form a part of a ring; and
- wherein the substituents  $\text{R}^{540}$ ,  $\text{R}^{541}$ ,  $\text{R}^{542}$ ,  $\text{R}^{543}$ ,  $\text{R}^{544}$ ,  $\text{R}^{545}$ ,  $\text{R}^{546}$ ,  $\text{R}^{547}$ ,  $\text{R}^{548}$ ,  $\text{R}^{549}$ ,  $\text{R}^{550}$ ,  $\text{R}^{551}$ ,  $\text{R}^{552}$ ,  $\text{R}^{553}$ ,  $\text{R}^{554}$ ,  $\text{R}^{555}$ ,  $\text{R}^{556}$ ,  $\text{R}^{557}$ ,  $\text{R}^{558}$ ,  $\text{R}^{559}$ ,  $\text{R}^{560}$ ,  $\text{R}^{561}$ , and  $\text{R}^{562}$ , independently of each other are a hydrogen atom ( $-\text{H}$ ), or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group;

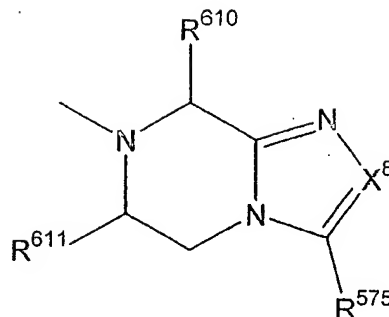
or wherein the group PM



has the formula (IX) or (IXa)



(IX)



(IXa)

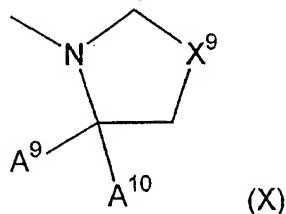
- wherein  $X^8$  is N or  $CR^{570}$ ; and
- wherein  $R^{570}$ ,  $R^{575}$ ,  $R^{610}$  and  $R^{611}$  independently of each other, are  
a hydrogen atom (-H); or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group or, a carbaldehyde (-CHO), a ketone group (-CO- $R^{580}$ ), a boronic acid group (-B(OH)<sub>2</sub>), a cyano group (-C≡N), a carboxylic acid group (-COOH), a carboxylic acid ester group (-COOR<sup>581</sup>), a carboxylic acid anhydride group (-CO-O-CO- $R^{582}$ ), a hydroxamic acid group (-CO-NH(OH)), a N-substituted hydroxamic acid group (-CO-NR<sup>583</sup>(OH)), a O-substituted hydroxamic acid group (-CO-NH(OR<sup>584</sup>)), a carboxamide group (-CO-NH<sub>2</sub>), a N-substituted or N,N-disubstituted carboxylic acid amide group, (-CO-NHR<sup>585</sup>; -CO-NR<sup>586</sup> $R^{587}$ ), an amido group (-HN-CO- $R^{588}$ ), a sulfonic acid group (-SO<sub>3</sub>H), a sulfonamide group (-SO<sub>2</sub>-NH<sub>2</sub>), a N-substituted or N,N-disubstituted sulfonamide group (-SO<sub>2</sub>-NHR<sup>589</sup>; -SO<sub>2</sub>-NR<sup>590</sup> $R^{591}$ ), an amidosulfone group (-NH-SO<sub>2</sub>- $R^{592}$ ), a sulfone group (-SO<sub>2</sub>- $R^{593}$ ), a phosphoric acid group (-OP(=O)(OH)<sub>2</sub>), a phosphoric acid ester group (-OP(=O)(OR<sup>594</sup>)(OR<sup>595</sup>)), a phosphonic acid group (-P(=O)(OH)<sub>2</sub>), an phosphonic acid ester group (-P(=O)(OR<sup>596</sup>)(OR<sup>597</sup>)), a halogen atom, a trifluormethyl group (-CF<sub>3</sub>), a thiol group (-SH); a thioether group (-S- $R^{598}$ ), a

hydroxy group (-OH); an alkoxy group (-O-R<sup>599</sup>), a tetrazole group, an amino group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted amino group (-NHR<sup>600</sup>; -NR<sup>601</sup>R<sup>602</sup>);

- which, independently of each other, can be substituted with one or more substituents, which can be the same or different; and,
- wherein optionally, the pairs R<sup>570</sup>/R<sup>575</sup>, if present, as well as the pairs R<sup>586</sup>/R<sup>587</sup>, R<sup>590</sup>/R<sup>591</sup>, R<sup>594</sup>/R<sup>595</sup>, R<sup>596</sup>/R<sup>597</sup> and R<sup>601</sup>/R<sup>602</sup>, independently of each other, may form a part of a ring; and
- wherein the substituents R<sup>580</sup>, R<sup>581</sup>, R<sup>582</sup>, R<sup>583</sup>, R<sup>584</sup>, R<sup>585</sup>, R<sup>586</sup>, R<sup>587</sup>, R<sup>588</sup>, R<sup>589</sup>, R<sup>590</sup>, R<sup>591</sup>, R<sup>592</sup>, R<sup>593</sup>, R<sup>594</sup>, R<sup>595</sup>, R<sup>596</sup>, R<sup>597</sup>, R<sup>598</sup>, R<sup>599</sup>, R<sup>600</sup>, R<sup>601</sup>, and R<sup>602</sup>, independently of each other are a hydrogen atom (-H), or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group;

or wherein the group PM

has the formula (X)



- wherein the groups X<sup>9</sup> is CR<sup>900</sup>R<sup>901</sup>, S, SO, SO<sub>2</sub> or NR<sup>902</sup>

- wherein  $R^{900}$ ,  $R^{901}$  and  $R^{902}$ , are, independently of each other, selected from hydrogen, fluorine,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens, or  $-C(=O)NR^{910}R^{911}$ .
- wherein  $A^9$  and  $A^{10}$  are, independently of each other, selected from hydrogen, cyano,  $-C(=O)NR^{912}R^{913}$ , or  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein

- $R^{910}$  and  $R^{912}$ , are, independently of each other, selected from hydrogen, or  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens; and
- $R^{911}$  and  $R^{913}$ , are, independently of each other, selected from the group consisting of

(1) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5, substituents independently selected from halogen and  $R^{920}$ ;

(2)  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6 or 7 substituents independently selected from (a) 0, 1, 2, 3, 4, or 5 halogens, and (b) 0, 1, 2 substituents selected from the group consisting of

- (a) hydroxy,
- (b)  $-COOH$ ,
- (c)  $-COO(C_1, C_2, C_3, C_4, C_5 \text{ or } C_6 \text{ alkyl})$ , i.e. ester,
- (d) phenyl,
- (e) naphthyl,
- (f)  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  cycloalkyl,
- (g) a 5 - or 6 membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur;

(h) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (a) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (b) a benzene ring fused to a 5- or 6-membered heterocycle having 1, 2, or 3 hetero atoms;

- wherein said C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl, phenyl, naphthyl, are optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from halogen and R<sup>920</sup>, and said 5 or 6 membered heterocycle and said 8, 9 or 10 - membered bicyclic ring system are each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from from oxo, hydroxy, halogen, and R<sup>920</sup>; and

(3) C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, which is optionally substituted with 1, 2, or 3 groups independently selected from halogen, hydroxy, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein R<sup>920</sup> is selected from the group consisting of:

(1) hydroxy;

(2) cyano;

(3) C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl optionally substituted with 1, 2, or 3 groups independently selected from halogen, hydroxy, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, wherein said -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl are linear or branched and are optionally substituted with 1, 2, 3, 4, 5 or 6 substituents selected from 1, 2, 3, 4, or 5 halogens, and 0 or 1 substituents selected from -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester,

-COOH, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl substituents being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(4) C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub>, C<sub>9</sub> or C<sub>10</sub> alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6, or 7 substituents independently selected from 0, 1, 2, 3, 4, or 5 halogen atoms and 0, 1, or 2 groups selected from

(a) hydroxy;

(b) -COOH;

(c) -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, which may linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens;

(d) a 5 - or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.;

(e) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (i) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (ii) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(f) -CONR<sup>925</sup>R<sup>925</sup>;

(g) -SO<sub>2</sub>NR<sup>925</sup>R<sup>925</sup>;

(h)  $-\text{NR}^{925}-\text{C}(=\text{O})\text{R}^{925}$

(i)  $-\text{NR}^{925}-\text{C}(=\text{O})\text{NR}^{925}\text{R}^{925}$ ;

(j)  $-\text{NR}^{925}\text{COOR}^{930}$

(k)  $-\text{O}-\text{CO}-\text{R}^{930}$

(l)  $-\text{O}-\text{CO}-\text{NR}^{925}\text{R}^{925}$ ;

(m)  $-\text{NR}^{925}\text{SO}_2\text{R}^{930}$ ;

(n)  $-\text{NR}^{925}\text{R}^{925}$ ;

(o) phenyl which is optionally substituted with 1, 2, 3, 4, or 5 group independently selected from halogen, hydroxy,  $\text{C}_1$ ,  $\text{C}_2$ ,  $\text{C}_3$ ,  $\text{C}_4$ ,  $\text{C}_5$  or  $\text{C}_6$  alkyl,  $-\text{OC}_1$ ,  $-\text{OC}_2$ ,  $-\text{OC}_3$ ,  $-\text{OC}_4$ ,  $-\text{OC}_5$  or  $-\text{OC}_6$  alkyl,  $-\text{COOH}$ ,  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester, said  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  alkyl,  $-\text{OC}_1$ ,  $-\text{OC}_2$ ,  $-\text{OC}_3$ ,  $-\text{OC}_4$ ,  $-\text{OC}_5$  or  $-\text{OC}_6$  alkyl,  $-\text{COOH}$ ,  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, 5, or 6 substituents independently selected from 0 or 1  $\text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  cycloalkyl and 0, 1, 2, 3, 4, or 5 halogens, and

(p)  $\text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  cycloalkyl, which is optionally substituted with 1, 2, 3, 4, 5, or 6 halogens;

(5)  $\text{OC}_1, \text{OC}_2, \text{OC}_3, \text{OC}_4, \text{OC}_5, \text{OC}_6, \text{OC}_7, \text{OC}_8, \text{OC}_9$  or  $\text{OC}_{10}$  alkyl, which is linear or branched and is optionally substituted with 0, 1, 2, 3, 4, or 5 halogen atoms and 0, 1, or 2 substituents selected from

(a) hydroxy;

(b)  $-\text{COOH}$ ;

(c)  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester, which may be linear or branched and is optionally substituted with 1, 2, 3, 4 or 5 halogens;

(d) a 5 - or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen,  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5$  or  $-\text{OC}_6$  alkyl, said  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5$  or  $-\text{OC}_6$  alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.;

(e) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (i) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (ii) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(f) -CONR<sup>925</sup>R<sup>925</sup>;

(g) -SO<sub>2</sub>NR<sup>925</sup>R<sup>925</sup>;

(h) -NR<sup>925</sup>-C(=O)R<sup>925</sup>

(i) -NR<sup>925</sup>-C(=O)NR<sup>925</sup>R<sup>925</sup>;

(j) -NR<sup>925</sup>COOR<sup>930</sup>

(k) -O-CO-R<sup>930</sup>

(l) -O-CO-NR<sup>925</sup>R<sup>925</sup>;

(m) -NR<sup>925</sup>SO<sub>2</sub>R<sup>930</sup>;

(n) -NR<sup>925</sup>R<sup>925</sup>;

(o) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5 groups independently selected from halogen, hydroxy, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, 5, or 6 substituents independently selected from 0 or 1 C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl and 0, 1, 2, 3, 4, or 5 halogens, and

(p) C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, which is optionally substituted with 1, 2, 3, 4, 5, or 6 halogens;

(6) -COOH;

- (7)  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester, which may be linear or branched and is optionally substituted with 1, 2, 3, 4, 5 halogens;
- (8) a 5 - or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, said heterocycle being optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen,  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5 \text{ or } -\text{OC}_6$  alkyl, said  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5 \text{ or } -\text{OC}_6$  alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.
- (9) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (a) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (b) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen,  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5 \text{ or } -\text{OC}_6$  alkyl, said  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5 \text{ or } -\text{OC}_6$  alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;
- (10)  $-\text{CONR}^{925}\text{R}^{925}$ ;
- (11)  $-\text{SO}_2\text{NR}^{925}\text{R}^{925}$ ;
- (12)  $-\text{NR}^{925}-\text{C}(=\text{O})\text{R}^{925}$
- (13)  $-\text{NR}^{925}-\text{C}(=\text{O})\text{NR}^{925}\text{R}^{925}$ ;
- (14)  $-\text{NR}^{925}\text{COOR}^{930}$
- (15)  $-\text{O}-\text{CO}-\text{R}^{930}$
- (16)  $-\text{O}-\text{CO}-\text{NR}^{925}\text{R}^{925}$ ;
- (17)  $-\text{NR}^{925}\text{SO}_2\text{R}^{930}$ ;
- (18)  $-\text{NR}^{925}\text{R}^{925}$ ;
- (19) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5 group independently selected from halogen, hydroxy,  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6$  alkyl,



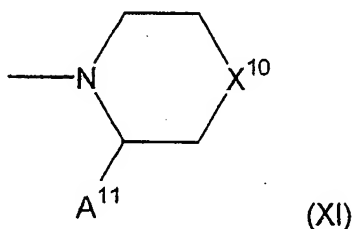
-OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein R<sup>930</sup> is selected from the group consisting of phenyl, C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, and C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, wherein C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6, substituents independently selected from 0, 1, 2, 3, 4, or 5 halogens, 0 or 1 phenyl, wherein said optional phenyl substituent and said R<sup>930</sup>, when R<sup>930</sup> is phenyl or C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, are optionally substituted with 1, 2, 3, 4, or 5 substituents, independently selected from halogen, OH, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, or C<sub>5</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, or -OC<sub>5</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, or C<sub>5</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, or -OC<sub>5</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.

wherein R<sup>925</sup> is selected from R<sup>930</sup> and hydrogen.

wherein the group PM

has the formula (XI)



wherein the groups X<sup>10</sup> is CR<sup>1000</sup>R<sup>1001</sup>, S, SO, SO<sub>2</sub> or NR<sup>1002</sup>

- wherein  $R^{1000}$ ,  $R^{1001}$  and  $R^{1002}$ , are, independently of each other, selected from hydrogen, fluorine,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens, or  $-C(=O)NR^{910}R^{911}$ .

and  $A^{11}$  is selected from

hydrogen, cyano,  $-C(=O)NR^{1012}R^{1013}$ , or  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein

- $R^{1010}$  and  $R^{1012}$ , are, independently of each other, selected from hydrogen, or  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens; and
- $R^{1011}$  and  $R^{1013}$ , are, independently of each other, selected from the group consisting of

(1) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5, substituents independently selected from halogen and  $R^{1020}$ ;

(2)  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6 or 7 substituents independently selected from (a) 0, 1, 2, 3, 4, or 5 halogens, and (b) 0, 1, 2 substituents selected from the group consisting of

- (a) hydroxy,
- (b)  $-COOH$ ,
- (c)  $-COO(C_1, C_2, C_3, C_4, C_5 \text{ or } C_6 \text{ alkyl})$ , i.e. ester,
- (d) phenyl,
- (e) naphthyl,
- (f)  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  cycloalkyl,
- (g) a 5 - or 6 membered htereocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 heteroatoms independently selected from nitrogen , oxygen or sulfur;

(h) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (a) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (b) a benzene ring fused to a 5- or 6-membered heterocycle having 1, 2, or 3 hetero atoms;

- wherein said C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl, phenyl, naphthyl, are optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from halogen and R<sup>1020</sup>, and said 5 or 6 membered heterocycle and said 8, 9 or 10 - membered bicyclic ring system are each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from from oxo, hydroxy, halogen, and R<sup>1020</sup>; and

(3) C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, which is optionally substituted with 1, 2, or 3 groups independently selected from halogen, hydroxy, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein R<sup>1020</sup> is selected from the group consisting of:

(1) hydroxy;

(2) cyano;

(3) C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl optionally substituted with 1, 2, or 3 groups independently selected from halogen, hydroxy, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, wherein said -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl are linear or branched and are optionally substituted with 1, 2, 3, 4, 5 or 6 substituents selected from 1, 2, 3, 4, or 5 halogens, and 0 or 1 substituents selected from -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester,

-COOH, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl substituents being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(4) C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub>, C<sub>9</sub> or C<sub>10</sub> alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6, or 7 substituents independently selected from 0, 1, 2, 3, 4, or 5 halogen atoms and 0, 1, or 2 groups selected from

(a) hydroxy;

(b) -COOH;

(c) -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, which may linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens;

(d) a 5 - or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.;

(e) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (i) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (ii) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(f) -CONR<sup>1025</sup>R<sup>1025</sup>;

(g) -SO<sub>2</sub>NR<sup>1025</sup>R<sup>1025</sup>;

(h)  $-NR^{1025}-C(=O)R^{1025}$

(i)  $-NR^{1025}-C(=O)NR^{1025}R^{1025}$ ;

(j)  $-NR^{1025}COOR^{1030}$

(k)  $-O-CO-R^{1030}$

(l)  $-O-CO-NR^{1025}R^{1025}$ ;

(m)  $-NR^{1025}SO_2R^{1030}$ ;

(n)  $-NR^{1025}R^{1025}$ ;

(o) phenyl which is optionally substituted with 1, 2, 3, 4, or 5 group independently selected from halogen, hydroxy,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl,  $-OC_1$ ,  $-OC_2$ ,  $-OC_3$ ,  $-OC_4$ ,  $-OC_5$  or  $-OC_6$  alkyl,  $-COOH$ ,  $-COO(C_1, C_2, C_3, C_4, C_5$  or  $C_6$  alkyl) i.e. ester, said  $C_1, C_2, C_3, C_4, C_5$  or  $C_6$  alkyl,  $-OC_1$ ,  $-OC_2$ ,  $-OC_3$ ,  $-OC_4$ ,  $-OC_5$  or  $-OC_6$  alkyl,  $-COOH$ ,  $-COO(C_1, C_2, C_3, C_4, C_5$  or  $C_6$  alkyl) i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, 5, or 6 substituents independently selected from 0 or 1  $C_3, C_4, C_5$  or  $C_6$  cycloalkyl and 0, 1, 2, 3, 4, or 5 halogens, and

(p)  $C_3, C_4, C_5$  or  $C_6$  cycloalkyl, which is optionally substituted with 1, 2, 3, 4, 5, or 6 halogens;

(5)  $OC_1, OC_2, OC_3, OC_4, OC_5, OC_6, OC_7, OC_8, OC_9$  or  $OC_{10}$  alkyl, which is linear or branched and is optionally substituted with 0, 1, 2, 3, 4, or 5 halogen atoms and 0, 1, or 2 substituents selected from

(a) hydroxy;

(b)  $-COOH$ ;

(c)  $-COO(C_1, C_2, C_3, C_4, C_5$  or  $C_6$  alkyl) i.e. ester, which may be linear or branched and is optionally substituted with 1, 2, 3, 4 or 5 halogens;

(d) a 5 - or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen,  $C_1, C_2, C_3, C_4, C_5$  or  $C_6$  alkyl, and  $-OC_1, -OC_2, -OC_3, -OC_4, -OC_5$  or  $-OC_6$  alkyl, said  $C_1, C_2, C_3, C_4, C_5$  or  $C_6$  alkyl, and  $-OC_1, -OC_2, -OC_3, -OC_4, -OC_5$  or  $-OC_6$  alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.;

(e) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (i) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (ii) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(f) -CONR<sup>1025</sup>R<sup>1025</sup>;

(g) -SO<sub>2</sub>NR<sup>1025</sup>R<sup>1025</sup>;

(h) -NR<sup>1025</sup>-C(=O)R<sup>1025</sup>

(i) -NR<sup>1025</sup>-C(=O)NR<sup>1025</sup>R<sup>1025</sup>;

(j) -NR<sup>1025</sup>COOR<sup>1030</sup>

(k) -O-CO-R<sup>1030</sup>

(l) -O-CO-NR<sup>1025</sup>R<sup>1025</sup>;

(m) -NR<sup>1025</sup>SO<sub>2</sub>R<sup>1030</sup>;

(n) -NR<sup>1025</sup>R<sup>1025</sup>;

(o) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5 groups independently selected from halogen, hydroxy, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, 5, or 6 substituents independently selected from 0 or 1 C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl and 0, 1, 2, 3, 4, or 5 halogens, and

(p) C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, which is optionally substituted with 1, 2, 3, 4, 5, or 6 halogens;

(6) -COOH;

(7)  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester, which may be linear or branched and is optionally substituted with 1, 2, 3, 4, 5 halogens;

(8) a 5 - or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, said heterocycle being optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen,  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5 \text{ or } -\text{OC}_6$  alkyl, said  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5 \text{ or } -\text{OC}_6$  alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.

(9) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (a) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (b) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen,  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5 \text{ or } -\text{OC}_6$  alkyl, said  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5 \text{ or } -\text{OC}_6$  alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(10)  $-\text{CONR}^{1025}\text{R}^{1025}$ ;

(11)  $-\text{SO}_2\text{NR}^{1025}\text{R}^{1025}$ ;

(12)  $-\text{NR}^{1025}-\text{C}(=\text{O})\text{R}^{1025}$

(13)  $-\text{NR}^{1025}-\text{C}(=\text{O})\text{NR}^{1025}\text{R}^{1025}$ ;

(14)  $-\text{NR}^{925}\text{COOR}^{1030}$

(15)  $-\text{O}-\text{CO}-\text{R}^{1030}$

(16)  $-\text{O}-\text{CO}-\text{NR}^{1025}\text{R}^{1025}$ ;

(17)  $-\text{NR}^{1025}\text{SO}_2\text{R}^{1030}$ ;

(18)  $-\text{NR}^{1025}\text{R}^{1025}$ ;

(19) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5 group independently selected from halogen, hydroxy,  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6$  alkyl,

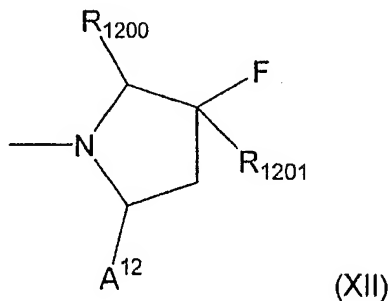
-OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein R<sup>1030</sup> is selected from the group consisting of phenyl, C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, and C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, wherein C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6, substituents independently selected from 0, 1, 2, 3, 4, or 5 halogens, 0 or 1 phenyl, wherein said optional phenyl substituent and said R<sup>930</sup>, when R<sup>930</sup> is phenyl or C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, are optionally substituted with 1, 2, 3, 4, or 5 substituents, independently selected from halogen, OH, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, or C<sub>5</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, or -OC<sub>5</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, or C<sub>5</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, or -OC<sub>5</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.

wherein R<sup>1025</sup> is selected from R<sup>1030</sup> and hydrogen.

or wherein the group PM

has the formula (XII)

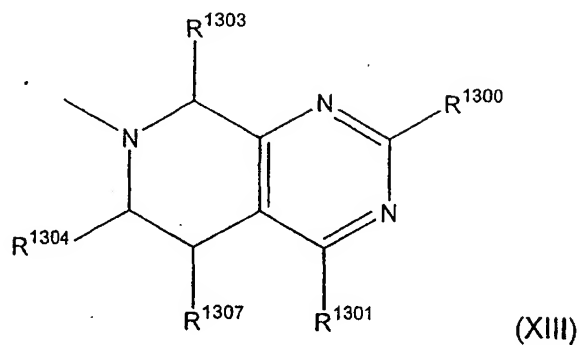




- wherein the groups  $R^{1201}$  is hydrogen or fluoro.
- wherein  $R^{1200}$  and  $A^{12}$  is selected from hydrogen and cyano, and the other is hydrogen.

or wherein the group PM

has the formula XIII:



wherein:

$R^{1300}$  and  $R^{1301}$  are independently selected from the group consisting of:

- (10) hydrogen,
- (11) CN,
- (12)  $C_{1-10}$ alkyl, which is linear or branched which is unsubstituted or substituted with:
  - a) halogen, or

- b) phenyl, which is unsubstituted or substituted with 1 - 5 substituents independently selected from halogen, CN, OH,  $R^{1302}$ ,  $OR^{1302}$ ,  $NHSO_2R^{1302}$ ,  $N(C_{1-6}alkyl)SO_2R^{1302}$ ,  $SO_2R^{1302}$ ,  $SO_2NR^{1305}R^{1306}$ ,  $NR^{1305}R^{1306}$ ,  $CONR^{1305}R^{1306}$ ,  $CO_2H$ , and  $CO_2C_{1-6}alkyl$ , wherein the  $C_{1-6}alkyl$  is linear or branched,
- (13) phenyl which is unsubstituted or substituted with 1 - 5 substituents independently selected from halogen, CN, OH,  $R^{1302}$ ,  $OR^{1302}$ ,  $NHSO_2R^{1302}$ ,  $N(C_{1-6}alkyl)SO_2R^{1302}$ ,  $SO_2R^{1302}$ ,  $SO_2NR^{1305}R^{1306}$ ,  $NR^{1305}R^{1306}$ ,  $CONR^{1305}R^{1306}$ ,  $CO_2H$ , and  $CO_2C_{1-6}alkyl$ , wherein the  $C_{1-6}alkyl$  is linear or branched,
- (14) a 5- or 6-membered heterocyclic which may be saturated or unsaturated comprising 1 - 4 heteroatoms independently selected from N, S and O, the heterocycle being unsubstituted or substituted with 1 - 3 substituents independently selected from oxo, halogen,  $NO_2$ , CN, OH,  $R^{1302}$ ,  $OR^{1302}$ ,  $NHSO_2R^{1302}$ ,  $N(C_{1-6}alkyl)SO_2R^{1302}$ ,  $SO_2R^{1302}$ ,  $SO_2NR^{1305}R^{1306}$ ,  $NR^{1305}R^{1306}$ ,  $CONR^{1305}R^{1306}$ ,  $CO_2H$ , and  $CO_2C_{1-6}alkyl$ , wherein the  $C_{1-6}alkyl$  is linear or branched,
- (15)  $C_{3-6}cycloalkyl$ , which is optionally substituted with 1 - 5 substituents independently selected from halogen, OH,  $C_{1-6}alkyl$ , and  $OC_{1-6}alkyl$ , wherein the  $C_{1-6}alkyl$  and  $OC_{1-6}alkyl$  are linear or branched and optionally substituted with 1 - 5 halogens,
- (16) OH,
- (17)  $OR^{1302}$ , and
- (18)  $NR^{1305}R^{1306}$ ,

$R^{1302}$  is  $C_{1-6}alkyl$ , which is linear or branched and which is unsubstituted or substituted with 1 - 5 groups independently selected from halogen,  $CO_2H$ , and  $CO_2C_{1-6}alkyl$ , wherein the  $C_{1-6}alkyl$  is linear or branched;

$R^{1303}$ ,  $R^{1304}$  and  $R^{1307}$  are independently selected from the group consisting of:

- (10) hydrogen,

- (11) C<sub>1-10</sub>alkyl, which is linear or branched and which is unsubstituted or substituted with one or more substituted selected from:
- a) halogen,
  - b) hydroxy,
  - c) phenyl, which is unsubstituted or substituted with 1 – 5 substituted independently selected from halogen, OH, C<sub>1-6</sub>alkyl, and OC<sub>1-6</sub>alkyl, wherein the C<sub>1-6</sub>alkyl is linear or branched and optionally substituted with 1 – 5 halogens,
  - d) naphthyl, wherein the naphthyl is optionally substituted with 1 – 5 substituents independently selected from halogen, OH, C<sub>1-6</sub>alkyl, and OC<sub>1-6</sub>alkyl, wherein the C<sub>1-6</sub>alkyl is linear or branched and optionally substituted with 1 – 5 halogens,
  - e) CO<sub>2</sub>H,
  - f) CO<sub>2</sub>C<sub>1-6</sub>alkyl,
  - g) CONR<sup>1305</sup>R<sup>1306</sup>,
- (12) CN,
- (13) phenyl which is unsubstituted or substituted with 1 – 5 substituents independently selected from C<sub>1-6</sub>alkyl, and OC<sub>1-6</sub>alkyl, hydroxy and halogen, wherein the C<sub>1-6</sub>alkyl is linear or branched and optionally substituted with 1 – 5 halogens,
- (14) naphthyl which is unsubstituted or substituted with 1 – 5 substituents independently selected from C<sub>1-6</sub>alkyl, and OC<sub>1-6</sub>alkyl, hydroxy and halogen, wherein the C<sub>1-6</sub>alkyl is linear or branched and optionally substituted with 1 – 5 halogens,
- (15) CO<sub>2</sub>H,
- (16) CO<sub>2</sub>C<sub>1-6</sub>alkyl,
- (17) CONR<sup>1305</sup>R<sup>1306</sup>, and
- (18) C<sub>3-6</sub>cycloalkyl, which is unsubstituted or substituted with 1 – 5 substituents independently selected from C<sub>1-6</sub>alkyl, and OC<sub>1-6</sub>alkyl, hydroxy and halogen, wherein the C<sub>1-6</sub>alkyl is linear or branched and optionally substituted with 1 – 5 halogens;

$R^{1305}$  and  $R^{1306}$  are independently selected from the group consisting of:

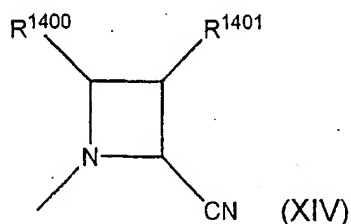
- (5) hydrogen,
- (6) phenyl, which is unsubstituted or substituted with substituents independently selected from halogen, OH,  $C_{1-6}$ alkyl, and  $OC_{1-6}$ alkyl, wherein the  $C_{1-6}$ alkyl is linear or branched and optionally substituted with 1 – 5 halogens,
- (7)  $C_{3-6}$ cycloalkyl, which is unsubstituted or substituted with 1 – 5 substituents independently selected from  $C_{1-6}$ alkyl, and  $OC_{1-6}$ alkyl, wherein the  $C_{1-6}$ alkyl is linear or branched and optionally substituted with 1 – 5 halogens,
- (8)  $C_{1-6}$ alkyl, which is linear or branched and which is unsubstituted or substituted with:

- a) halogen, or
- b) phenyl, which is unsubstituted or substituted with 1 – 5 substituents independently selected from halogen, OH,  $C_{1-6}$ alkyl, and  $OC_{1-6}$ alkyl, wherein the  $C_{1-6}$ alkyl is linear or branched and optionally substituted with 1 – 5 halogens,

or wherein  $R^{1305}$  and  $R^{1306}$  together with the nitrogen atom to which they are attached form a heterocyclic ring selected from azetidine, pyrrolidine, piperidine, piperazine, and morpholine wherein said heterocyclic ring is unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy,  $C_{1-6}$ alkyl, and  $C_{1-6}$ alkoxy, wherein alkyl and alkoxy are unsubstituted with one to five halogens;

or wherein the group PM

has the formula XIV:

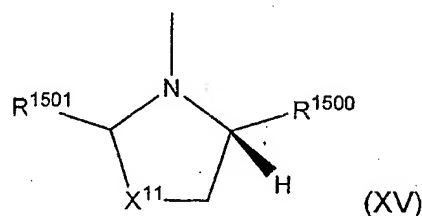


- wherein  $R^{1400}$  and  $R^{1401}$ , independently of each other, are
- a hydrogen atom (-H); or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group or, a carbaldehyde (-CHO), a ketone group (-CO- $R^{1402}$ ), a boronic acid group (-B(OH)<sub>2</sub>), a cyano group (-C≡N), a carboxylic acid group (-COOH), a carboxylic acid ester group (-COOR<sup>1403</sup>), a carboxylic acid anhydride group (-CO-O-CO- $R^{1404}$ ), a hydroxamic acid group (-CO-NH(OH)), a N-substituted hydroxamic acid group (-CO-NR<sup>1405</sup>(OH)), a O-substituted hydroxamic acid group (-CO-NH(OR<sup>1406</sup>)), a carboxamide group (-CO-NH<sub>2</sub>), a N-substituted or N,N-disubstituted carboxylic acid amide group, (-CO-NHR<sup>1407</sup>; -CO-NR<sup>1408</sup>R<sup>1409</sup>), an amido group (-HN-CO- $R^{1410}$ ), a sulfonic acid group (-SO<sub>3</sub>H), a sulfonamide group (-SO<sub>2</sub>-NH<sub>2</sub>), a N-substituted or N,N-disubstituted sulfonamide group (-SO<sub>2</sub>-NHR<sup>1411</sup>; -SO<sub>2</sub>-NR<sup>1412</sup>R<sup>1413</sup>), an amidosulfone group (-NH-SO<sub>2</sub>- $R^{1414}$ ), a sulfone group (-SO<sub>2</sub>- $R^{1415}$ ), a phosphoric acid group (-OP(=O)(OH)<sub>2</sub>), a phosphoric acid ester group (-OP(=O)(OR<sup>1416</sup>)(OR<sup>1417</sup>)), a phosphonic acid group (-P(=O)(OH)<sub>2</sub>), an phosphonic acid ester group (-P(=O)(OR<sup>1418</sup>)(OR<sup>1419</sup>)), a halogen atom, a trifluormethyl group (-CF<sub>3</sub>), a thiol group (-SH); a thioether group (-S- $R^{1420}$ ), a hydroxy group (-OH); an alkoxy group (-O- $R^{1421}$ ), a tetrazole group, an amino group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted amino group (-NHR<sup>1422</sup>; -NR<sup>1423</sup>R<sup>1424</sup>); and
- which, independently of each other, can be substituted with one or more substituents, which can be the same or different; and,
- wherein optionally, the pairs  $R^{1408}/R^{1409}$ ,  $R^{1412}/R^{1413}$ ,  $R^{1416}/R^{1417}$ ,  $R^{1418}/R^{1419}$  and  $R^{1423}/R^{1424}$ , independently of each other, may form a part of a ring; and
- wherein the substituents  $R^{1402}$ ,  $R^{1403}$ ,  $R^{1404}$ ,  $R^{1405}$ ,  $R^{1406}$ ,  $R^{1407}$ ,  $R^{1408}$ ,  $R^{1409}$ ,  $R^{1410}$ ,  $R^{1411}$ ,  $R^{1412}$ ,  $R^{1413}$ ,  $R^{1414}$ ,  $R^{1415}$ ,  $R^{1416}$ ,  $R^{1417}$ ,  $R^{1418}$ ,  $R^{1419}$ ,  $R^{1420}$ ,  $R^{1421}$ ,  $R^{1422}$ ,

$R^{1423}$ , and  $R^{1424}$ , independently of each other are a **hydrogen** atom (-H), or an **alkyl**, **alkenyl**, **alkynyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkynyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkynyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

or wherein the group PM

has the formula XV:



- wherein  $X^{11}$  is  $CH_2$ ,  $CHF$  or  $CF_2$ ;
- wherein  $R^{1500}$  is selected from the group consisting of alkylcarbonyl, arylcarbonyl, cyano, heterocyclecarbonyl,  $R^{1502}R^{1503}NC(O)-$ ,  $B(OR^{1504})_2$ , (1,2,3)-dioxaborolane and 4,4,5,5-tetramethyl(1,2,3)-dioxaborolane;
- wherein  $R^{1501}$  is selected from the group consisting of alkoxyalkyl, alkyl, alkylcarbonyl, alkenyl, alkynyl, allenyl, arylalkyl, cycloalkyl, cycloalkylalkyl, cyano, haloalkyl, haloalkenyl, heterocyclealkyl, and hydroxyalkyl;
- wherein  $R^{1502}$ ,  $R^{1503}$  and  $R^{1504}$  are each independently selected from the group consisting of hydrogen, alkyl, and arylalkyl;

with the proviso that the following compounds are excluded:

glutamin-thiazolidin (=Gln-Thia), glutamin-pyrrolidin (=Gln-Pyrr) (from WO 03/072556), glutamin-pyrrolidin-2-carboxylic acid (= Gln-Pro), glutamin-pyrrolidin-2-carboxamid (=Gln-Pro amid), and (S,S) 4-Amino-5-(2-cyano-2,5-dihydro-pyrrol-1-yl)-6-oxo-pentanoic acid amide (Gln - 2-cyano-2,5-dihydro-pyrrolidin) (from WO 01/55105).

## 2. Compound according to claim 1

wherein n is 0 or 1;

wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup>, and R<sup>11</sup> independently of each other are

- a **hydrogen** atom; or
- a substituted or unsubstituted **alkyl** group having 1 to 30 carbon atoms; or
- a substituted or unsubstituted **alkenyl** group having 2 to 30 carbon atoms; or
- a substituted or unsubstituted **alkinyl** group having 2 to 30 carbon atoms; or
- a substituted or unsubstituted **cycloalkyl** group having 3 to 30 carbon atoms; or
- a substituted or unsubstituted **cycloalkenyl** group having 3 to 30 carbon atoms;
- or a substituted or unsubstituted **cycloalkinyl** group having 6 to 30 carbon atoms; or
- a substituted or unsubstituted **heteroalkyl** group having 1 to 30 carbon atoms and 1 to 6 hetero atoms each independently selected from oxygen, nitrogen or sulfur; or
- a substituted or unsubstituted **heteroalkenyl** group having 2 to 30 carbon atoms and 1 to 6 hetero atoms each independently selected from oxygen, nitrogen or sulfur; or
- a substituted or unsubstituted **heteroalkinyl** group having 2 to 30 carbon atoms and 1 to 6 hetero atoms each independently selected from oxygen, nitrogen or sulfur; or
- a substituted or unsubstituted **heterocycloalkyl** group having 1 to 30 carbon atoms, and 1 to 6 hetero atoms each independently selected from oxygen, nitrogen or sulfur; or
- a substituted or unsubstituted **heterocycloalkenyl** group having 2 to 30 carbon atoms, and 1 to 6 hetero atoms each independently selected from oxygen, nitrogen or sulfur; or
- a substituted or unsubstituted **aryl** group having 3 to 30 carbon atoms; or
- a substituted or unsubstituted **heteroaryl** group having 1 to 30 carbon atoms, and 1 to 10 hetero atoms, each independently selected from oxygen, nitrogen or sulfur; or

- a substituted or unsubstituted **aryl-alkyl** group having at least one substituted or unsubstituted aryl group each having 1 to 30 carbon atoms, and at least one substituted or unsubstituted alkyl group each having 1 to 30 carbon atoms; or
- a substituted or unsubstituted **heteroaryl-alkyl** group having at least one substituted or unsubstituted heteroaryl group each having 1 to 30 carbon atoms, and 1 to 10 hetero atoms, each independently selected from oxygen, nitrogen or sulfur, and further, at least one substituted or unsubstituted alkyl group having having 1 to 30 carbon atoms; or
- a substituted or unsubstituted **aryl-heteroalkyl** group having at least one substituted or unsubstituted aryl group each having 3 to 30 carbon atoms, and at least one substituted or unsubstituted heteroalkyl group each having 1 to 30 carbon atoms and 1 to 6 hetero atoms each independently selected from oxygen, nitrogen or sulfur; or
- a substituted or unsubstituted **heteroaryl-heteroalkyl** group having at least one substituted or unsubstituted heteroaryl group each having 1 to 30 carbon atoms, and 1 to 10 hetero atoms, each independently selected from oxygen, nitrogen or sulfur, and further, at least one substituted or unsubstituted heteroalkyl group each having 1 to 30 carbon atoms and 1 to 6 hetero atoms each independently selected from oxygen, nitrogen or sulfur; or
- a **carbaldehyde** (-CHO), a **ketone** group (-CO-R<sup>20</sup>), a **boronic acid** group (-B(OH)<sub>2</sub>), a **cyano** group (-C≡N), a **carboxylic acid** group (-COOH), a **carboxylic acid ester** group (-COOR<sup>21</sup>), a **carboxylic acid anhydride** group (-CO-O-CO-R<sup>22</sup>), a **hydroxamic acid** group (-CO-NH(OH)), a N-substituted **hydroxamic acid** group (-CO-NR<sup>23</sup>(OH)), a O-substituted **hydroxamic acid** group (-CO-NH(OR<sup>24</sup>)), a **carboxamide** group (-CO-NH<sub>2</sub>), a N-substituted or N,N-disubstituted **carboxylic acid amide** group, (-CO-NHR<sup>25</sup>; -CO-NR<sup>26</sup>R<sup>27</sup>), an **amido** group (-HN-CO-R<sup>28</sup>), a **sulfonic acid** group (-SO<sub>3</sub>H), a **sulfonamide** group (-SO<sub>2</sub>-NH<sub>2</sub>), a N-substituted or N,N-disubstituted **sulfonamide** group (-SO<sub>2</sub>-NHR<sup>29</sup>; -SO<sub>2</sub>-NR<sup>30</sup>R<sup>31</sup>), an **amidosulfone** group (-NH-SO<sub>2</sub>-R<sup>32</sup>), a **sulfone** group (-SO<sub>2</sub>-R<sup>33</sup>), a **phosphoric acid** group (-OP(=O)(OH)<sub>2</sub>), a **phosphoric acid ester** group (-OP(=O)(OR<sup>34</sup>)(OR<sup>35</sup>)), a **phosphonic acid** group (-P(=O)(OH)<sub>2</sub>), an **phosphonic acid ester** group (-P(=O)(OR<sup>36</sup>)(OR<sup>37</sup>)), a **halogen atom**, a



trifluormethyl group ( $-\text{CF}_3$ ), a thiol group ( $-\text{SH}$ ); a thioether group ( $-\text{S}-\text{R}^{38}$ ), a hydroxy group ( $-\text{OH}$ ); an alkoxy group ( $-\text{O}-\text{R}^{39}$ ), a tetrazole group, an amino group ( $-\text{NH}_2$ ), or a N-substituted or N,N-disubstituted amino group ( $-\text{NHR}^{40}$ ,  $-\text{NR}^{41}\text{R}^{42}$ );

- which each independently can be substituted with one or more substituents, which can be the same or different; and,
- wherein optionally, any two of the groups  $\text{R}^1, \text{R}^2, \text{R}^3, \text{R}^4, \text{R}^5, \text{R}^6, \text{R}^7, \text{R}^8, \text{R}^9, \text{R}^{10}$ , and  $\text{R}^{11}$ , as well the pairs  $\text{R}^{26}/\text{R}^{27}$ ,  $\text{R}^{30}/\text{R}^{31}$ ,  $\text{R}^{34}/\text{R}^{35}$ ,  $\text{R}^{36}/\text{R}^{37}$  and  $\text{R}^{41}/\text{R}^{42}$ , independently of each other, may form a part of a ring; and
- wherein the substituents  $\text{R}^{20}, \text{R}^{21}, \text{R}^{22}, \text{R}^{23}, \text{R}^{24}, \text{R}^{25}, \text{R}^{26}, \text{R}^{27}, \text{R}^{28}, \text{R}^{29}, \text{R}^{30}, \text{R}^{31}, \text{R}^{32}, \text{R}^{33}, \text{R}^{34}, \text{R}^{35}, \text{R}^{36}, \text{R}^{37}, \text{R}^{38}, \text{R}^{39}, \text{R}^{40}, \text{R}^{41}$ , and  $\text{R}^{42}$  independently of each other are a hydrogen atom ( $-\text{H}$ ), or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, heteroalkyl, heteroalkenyl, heteroalkynyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group.

### 3. Compound according to claims 1 or 2

wherein n is 0 or 1;

wherein  $\text{R}^1, \text{R}^2, \text{R}^3, \text{R}^4, \text{R}^5, \text{R}^6, \text{R}^7, \text{R}^8, \text{R}^9, \text{R}^{10}$ , and  $\text{R}^{11}$  independently of each other are

- a hydrogen atom; or
- a substituted or unsubstituted alkyl group having 1 to 20 carbon atoms; or
- a substituted or unsubstituted alkenyl group having 2 to 20 carbon atoms; or
- a substituted or unsubstituted alkynyl group having 2 to 20 carbon atoms; or
- a substituted or unsubstituted cycloalkyl group having 3 to 20 carbon atoms; or
- a substituted or unsubstituted cycloalkenyl group having 3 to 20 carbon atoms;

- or a substituted or unsubstituted **cycloalkinyl** group having 6 to 20 carbon atoms; or
- a substituted or unsubstituted **heteroalkyl** group having 1 to 20 carbon atoms and 1 to 3 hetero atoms each independently selected from oxygen, nitrogen or sulfur; or
- a substituted or unsubstituted **heteroalkenyl** group having 2 to 20 carbon atoms and 1 to 3 hetero atoms each independently selected from oxygen, nitrogen or sulfur; or
- a substituted or unsubstituted **heteroalkinyl** group having 2 to 20 carbon atoms and 1 to 3 hetero atoms each independently selected from oxygen, nitrogen or sulfur; or
- a substituted or unsubstituted **heterocycloalkyl** group having 1 to 20 carbon atoms, and 1 to 3 hetero atoms each independently selected from oxygen, nitrogen or sulfur; or
- a substituted or unsubstituted **heterocycloalkenyl** group having 2 to 20 carbon atoms, and 1 to 3 hetero atoms each independently selected from oxygen, nitrogen or sulfur; or
- a substituted or unsubstituted **aryl** group having 3 to 20 carbon atoms; or
- a substituted or unsubstituted **heteroaryl** group having 1 to 20 carbon atoms, and 1 to 4 hetero atoms, each independently selected from oxygen, nitrogen or sulfur; or
- a substituted or unsubstituted **aryl-alkyl** group having at least one substituted or unsubstituted aryl group each having 1 to 20 carbon atoms, and at least one substituted or unsubstituted alkyl group each having 1 to 20 carbon atoms; or
- a substituted or unsubstituted **heteroaryl-alkyl** group having at least one substituted or unsubstituted heteroaryl group each having 1 to 20 carbon atoms, and 1 to 4 hetero atoms, each independently selected from oxygen, nitrogen or sulfur, and further, at least one substituted or unsubstituted alkyl group having 1 to 20 carbon atoms; or
- a substituted or unsubstituted **aryl-heteroalkyl** group having at least one substituted or unsubstituted aryl group each having 3 to 20 carbon atoms, and at least one substituted or unsubstituted heteroalkyl group each having 1 to 20

- carbon atoms and 1 to 3 hetero atoms each independently selected from oxygen, nitrogen or sulfur; or
- a substituted or unsubstituted **heteroaryl-heteroalkyl** group having at least one substituted or unsubstituted heteroaryl group each having 1 to 20 carbon atoms, and 1 to 4 hetero atoms, each independently selected from oxygen, nitrogen or sulfur, and further, at least one substituted or unsubstituted heteroalkyl group each having 1 to 20 carbon atoms and 1 to 4 hetero atoms each independently selected from oxygen, nitrogen or sulfur; or
  - a **carbaldehyde** (-CHO), a **ketone** group (-CO-R<sup>20</sup>), a **boronic acid** group (-B(OH)<sub>2</sub>), a **cyano** group (-C≡N), a **carboxylic acid** group (-COOH), a **carboxylic acid ester** group (-COOR<sup>21</sup>), a **carboxylic acid anhydride** group (-CO-O-CO-R<sup>22</sup>), a **hydroxamic acid** group (-CO-NH(OH)), a N-substituted **hydroxamic acid** group (-CO-NR<sup>23</sup>(OH)), a O-substituted **hydroxamic acid** group (-CO-NH(OR<sup>24</sup>)), a **carboxamide** group (-CO-NH<sub>2</sub>), a N-substituted or N,N-disubstituted **carboxylic acid amide** group, (-CO-NHR<sup>25</sup>; -CO-NR<sup>26</sup>R<sup>27</sup>), an **amido** group (-HN-CO-R<sup>28</sup>), a **sulfonic acid** group (-SO<sub>3</sub>H), a **sulfonamide** group (-SO<sub>2</sub>-NH<sub>2</sub>), a N-substituted or N,N-disubstituted **sulfonamide** group (-SO<sub>2</sub>-NHR<sup>29</sup>; -SO<sub>2</sub>-NR<sup>30</sup>R<sup>31</sup>), an **amidosulfone** group (-NH-SO<sub>2</sub>-R<sup>32</sup>), a **sulfone** group (-SO<sub>2</sub>-R<sup>33</sup>), a **phosphoric acid** group (-OP(=O)(OH)<sub>2</sub>), a **phosphoric acid ester** group (-OP(=O)(OR<sup>34</sup>)(OR<sup>35</sup>)), a **phosphonic acid** group (-P(=O)(OH)<sub>2</sub>), an **phosphonic acid ester** group (-P(=O)(OR<sup>36</sup>)(OR<sup>37</sup>)), a **halogen atom**, a **trifluormethyl** group (-CF<sub>3</sub>), a **thiol** group (-SH); a **thioether** group (-S-R<sup>38</sup>), a **hydroxy** group (-OH); an **alkoxy** group (-O-R<sup>39</sup>), a **tetrazole** group, an **amino** group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted **amino** group (-NHR<sup>40</sup>; -NR<sup>41</sup>R<sup>42</sup>);
  - which each independently can be **substituted** with one or more substituents, which can be the same or different; and,
  - wherein optionally, any **two of the groups** R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup>, and R<sup>11</sup>, as well the pairs R<sup>26</sup>/R<sup>27</sup>, R<sup>30</sup>/R<sup>31</sup>, R<sup>34</sup>/R<sup>35</sup>, R<sup>36</sup>/R<sup>37</sup> and R<sup>41</sup>/R<sup>42</sup>, independently of each other, may form a part of a **ring**; and

- wherein the substituents  $R^{20}$ ,  $R^{21}$ ,  $R^{22}$ ,  $R^{23}$ ,  $R^{24}$ ,  $R^{25}$ ,  $R^{26}$ ,  $R^{27}$ ,  $R^{28}$ ,  $R^{29}$ ,  $R^{30}$ ,  $R^{31}$ ,  $R^{32}$ ,  $R^{33}$ ,  $R^{34}$ ,  $R^{35}$ ,  $R^{36}$ ,  $R^{37}$ ,  $R^{38}$ ,  $R^{39}$ ,  $R^{40}$ ,  $R^{41}$ , and  $R^{42}$  independently of each other are a **hydrogen** atom (-H), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group.

4. Compound according to claim 1, 2 or 3,

wherein n is 0 or 1;

wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ , and  $R^{11}$  independently of each other are

- a **hydrogen** atom; or
- a straight or branched chain, substituted or unsubstituted **alkyl** group comprising methyl ( $-CH_3$ ) and ethyl ( $-C_2H_5$ ); or
- a **halogen** comprising a fluoro, chloro, bromo or iodo atom; or
- a **cyano** group; a **thiol** group; a **hydroxy** group; a **carboxyl** group, a **tetrazole** group, an **amino** group; an **amido** group;

and wherein EWG1 and EWG2 is a double bound oxygen (=O).

5. Compound according to claim 1, 2, 3 or 4,

- wherein n is 0;
- wherein  $R^1$ ,  $R^2$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ , and  $R^{11}$ , is each a **hydrogen** atom; and
- wherein EWG1 and EWG2 is a **double bound oxygen** (=O).

6. Compound according to claim 1, 2, 3 or 4,

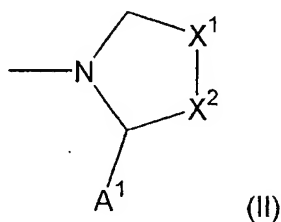
- wherein n is 1;

- wherein  $R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}$ , and  $R^{11}$  is each a **hydrogen** atom; and
- wherein EWG1 and EWG2 is a **double bound oxygen (=O)**.

7. Compound according to claims 1, 2, 3, 4, 5, and/or 6

wherein the group **PM**

has the formula (II)



- wherein  $X^1$  is  $CR^{51}R^{52}$ , O, S, or  $NR^{53}$ ; and
- wherein  $X^2$  is  $CR^{54}R^{55}$ , O, S, or  $NR^{56}$ ; and

wherein  $R^{51}, R^{52}, R^{53}, R^{54}, R^{55}$ , and  $R^{56}$ , independently of each other, are

- a **hydrogen** atom (-H); or an  $C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8$  and  $C_9$  branched or straight chain **alkyl**,  $C_2, C_3, C_4, C_5, C_6, C_7, C_8$  and  $C_9$  branched or straight chain **alkenyl**,  $C_2, C_3, C_4, C_5, C_6, C_7, C_8$  and  $C_9$  branched or straight chain **alkinyl**,  $C_3, C_4, C_5, C_6, C_7, C_8$  and  $C_9$  **cycloalkyl**,  $C_5, C_6, C_7, C_8$  and  $C_9$  **cycloalkenyl**, **aryl**, **heteroaryl** or **amino** ( $-NH_2$ ), or a N-substituted or N,N-disubstituted **amino** group ( $-NHR^{80}$ ;  $-NR^{81}R^{82}$ ); and
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,

- wherein optionally, any **two of the groups**  $R^{51}$ ,  $R^{52}$ ,  $R^{53}$ ,  $R^{54}$ ,  $R^{55}$ , and  $R^{56}$ , if present, as well as the pairs  $R^{66}/R^{67}$ ,  $R^{70}/R^{71}$ ,  $R^{74}/R^{75}$ ,  $R^{76}/R^{77}$  and  $R^{81}/R^{82}$ , independently of each other, may form a part of a **ring**; and
- wherein the substituents  $R^{60}$ ,  $R^{61}$ ,  $R^{62}$ ,  $R^{63}$ ,  $R^{64}$ ,  $R^{65}$ ,  $R^{66}$ ,  $R^{67}$ ,  $R^{68}$ ,  $R^{69}$ ,  $R^{70}$ ,  $R^{71}$ ,  $R^{72}$ ,  $R^{73}$ ,  $R^{74}$ ,  $R^{75}$ ,  $R^{76}$ ,  $R^{77}$ ,  $R^{78}$ ,  $R^{79}$ ,  $R^{80}$ ,  $R^{81}$ , and  $R^{82}$ , independently of each other, are a **hydrogen atom** (-H), or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkyl**, **aryl**, **heteroaryl**, **amino**, **halo**, **carbonyl**,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkoxy**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkenoxy**, **phenyloxy**, **benzyloxy**,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  **cycloalkyl**, **cyano**, **amido**, **thiol** **trifluoromethyl**, or **hydroxy** group; and

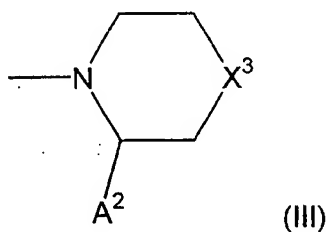
wherein  $A^1$  is

- a **hydrogen atom** (-H) or a **carbaldehyde** (-CHO), a **ketone** group (-CO- $R^{100}$ ), a **boronic acid** group (-B(OH)<sub>2</sub>), a **cyano** group (-C≡N), a **carboxylic acid** group (-COOH), a **carboxylic acid ester** group (-COOR<sup>101</sup>), a **carboxylic acid anhydride** group (-CO-O-CO- $R^{102}$ ), a **hydroxamic acid** group (-CO-NH(OH)), a **N-substituted hydroxamic acid** group (-CO-NR<sup>103</sup>(OH)), a **O-substituted hydroxamic acid** group (-CO-NH(OR<sup>104</sup>)), a **carboxamide** group (-CO-NH<sub>2</sub>), a **N-substituted or N,N-disubstituted carboxylic acid amide** group, (-CO-NHR<sup>105</sup>; -CO-NR<sup>106</sup>R<sup>107</sup>), an **amido** group (-HN-CO- $R^{108}$ ), a **sulfonic acid** group (-SO<sub>3</sub>H), a **sulfonamide** group (-SO<sub>2</sub>-NH<sub>2</sub>), a **N-substituted or N,N-disubstituted sulfonamide** group (-SO<sub>2</sub>-NHR<sup>109</sup>; -SO<sub>2</sub>-NR<sup>110</sup>R<sup>111</sup>), an **amidosulfone** group (-NH-SO<sub>2</sub>- $R^{112}$ ), a **sulfone** group (-SO<sub>2</sub>- $R^{113}$ ), a **phosphoric acid** group (-OP(=O)(OH)<sub>2</sub>), a **phosphoric acid ester** group (-OP(=O)(OR<sup>114</sup>)(OR<sup>115</sup>)), a **phosphonic acid** group (-P(=O)(OH)<sub>2</sub>), an **phosphonic acid ester** group (-P(=O)(OR<sup>116</sup>)(OR<sup>117</sup>)), a **halogen atom**, a **trifluormethyl** group (-CF<sub>3</sub>), a **thiol** group (-SH), a **thioether** group (-S- $R^{118}$ ), a **hydroxy** group (-OH), an **alkoxy** group (-O- $R^{119}$ ), a **tetrazole** group, an **amino** group (-NH<sub>2</sub>), or a **N-substituted or N,N-disubstituted amino** group (-NHR<sup>120</sup>; -NR<sup>121</sup>R<sup>122</sup>); and

- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the pairs  $R^{106}/R^{107}$ ,  $R^{110}/R^{111}$ ,  $R^{114}/R^{115}$ ,  $R^{116}/R^{117}$  and  $R^{121}/R^{122}$ , independently of each other, may form a part of a **ring**; and
- wherein the substituents  $R^{100}$ ,  $R^{101}$ ,  $R^{102}$ ,  $R^{103}$ ,  $R^{104}$ ,  $R^{105}$ ,  $R^{106}$ ,  $R^{107}$ ,  $R^{108}$ ,  $R^{109}$ ,  $R^{110}$ ,  $R^{111}$ ,  $R^{112}$ ,  $R^{113}$ ,  $R^{114}$ ,  $R^{115}$ ,  $R^{116}$ ,  $R^{117}$ ,  $R^{118}$ ,  $R^{119}$ ,  $R^{120}$ ,  $R^{121}$ , and  $R^{122}$ , independently of each other, are a **hydrogen** atom (-H), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

or wherein the group PM

has the formula (III)



- wherein  $X^3$  is  $CR^{131}R^{132}$ , O, S, or  $NR^{133}$ ; and
- wherein  $R^{131}$ ,  $R^{132}$ , and  $R^{133}$ , independently of each other, are
- a **hydrogen** atom (-H); or an  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkenyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkinyl**,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  **cycloalkyl**,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  **cycloalkenyl**, **aryl**, **heteroaryl** or an **amino** group ( $-NH_2$ ), or a N-substituted or N,N-disubstituted **amino** group ( $-NHR^{160}$ ;  $-NR^{161}R^{162}$ ); and

- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; and,
- wherein optionally, the **the pair**  $R^{131}/R^{132}$ , if present, as well the pairs  $R^{146}/R^{147}$ ,  $R^{150}/R^{151}$ ,  $R^{154}/R^{155}$ ,  $R^{156}/R^{157}$  and  $R^{161}/R^{162}$ , independently of each other, may form a part of a **ring**; and
- wherein the substituents  $R^{140}$ ,  $R^{141}$ ,  $R^{142}$ ,  $R^{143}$ ,  $R^{144}$ ,  $R^{145}$ ,  $R^{146}$ ,  $R^{147}$ ,  $R^{148}$ ,  $R^{149}$ ,  $R^{150}$ ,  $R^{151}$ ,  $R^{152}$ ,  $R^{153}$ ,  $R^{154}$ ,  $R^{155}$ ,  $R^{156}$ ,  $R^{157}$ ,  $R^{158}$ ,  $R^{159}$ ,  $R^{160}$ ,  $R^{161}$ , and  $R^{162}$ , independently of each other are a **hydrogen** atom (-H), or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkyl**, **aryl**, **heteroaryl**, **amino**, **halo**, **carbonyl**,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkoxy**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkenoxy**, **phenyloxy**, **benzyloxy**,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  **cycloalkyl**, **cyano**, **amido**, **thiol**, **trifluoromethyl**, or **hydroxy** group; and

wherein  $A^2$  is

- a **hydrogen** atom (-H); or a **carbaldehyde** (-CHO), a **ketone** group (-CO- $R^{180}$ ), a **boronic acid** group (-B(OH)<sub>2</sub>), a **cyano** group (-C≡N), a **carboxylic acid** group (-COOH), a **carboxylic acid ester** group (-COOR<sup>181</sup>), a **carboxylic acid anhydride** group (-CO-O-CO- $R^{182}$ ), a **hydroxamic acid** group (-CO-NH(OH)), a **N-substituted hydroxamic acid** group (-CO-NR<sup>183</sup>(OH)), a **O-substituted hydroxamic acid** group (-CO-NH(OR<sup>184</sup>)), a **carboxamide** group (-CO-NH<sub>2</sub>), a **N-substituted or N,N-disubstituted carboxylic acid amide** group, (-CO-NHR<sup>185</sup>; -CO-NR<sup>186</sup>R<sup>187</sup>), an **amido** group (-HN-CO- $R^{188}$ ), a **sulfonic acid** group (-SO<sub>3</sub>H), a **sulfonamide** group (-SO<sub>2</sub>-NH<sub>2</sub>), a **N-substituted or N,N-disubstituted sulfonamide** group (-SO<sub>2</sub>-NHR<sup>189</sup>; -SO<sub>2</sub>-NR<sup>190</sup>R<sup>191</sup>), an **amidosulfone** group (-NH-SO<sub>2</sub>- $R^{192}$ ), a **sulfone** group (-SO<sub>2</sub>- $R^{193}$ ), a **phosphoric acid** group (-OP(=O)(OH)<sub>2</sub>), a **phosphoric acid ester** group (-OP(=O)(OR<sup>194</sup>)(OR<sup>195</sup>)), a **phosphonic acid** group (-P(=O)(OH)<sub>2</sub>), an **phosphonic acid ester** group (-P(=O)(OR<sup>196</sup>)(OR<sup>197</sup>)), a **halogen atom**, a **trifluormethyl** group (-CF<sub>3</sub>), a **thiol**

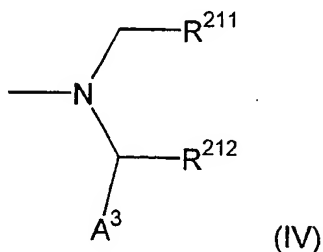


group (-SH); a **thioether** group (-S-R<sup>198</sup>), a **hydroxy** group (-OH); an **alkoxy** group (-O-R<sup>199</sup>), a **tetrazole** group, an **amino** group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted **amino** group (-NHR<sup>200</sup>, -NR<sup>201</sup>R<sup>202</sup>); and

- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the pairs R<sup>186</sup>/R<sup>187</sup>, R<sup>190</sup>/R<sup>191</sup>, R<sup>194</sup>/R<sup>195</sup>, R<sup>196</sup>/R<sup>197</sup> and R<sup>201</sup>/R<sup>202</sup> independently of each other, may form a part of a **ring**; and
- wherein the substituents R<sup>180</sup>, R<sup>181</sup>, R<sup>182</sup>, R<sup>183</sup>, R<sup>184</sup>, R<sup>185</sup>, R<sup>186</sup>, R<sup>187</sup>, R<sup>188</sup>, R<sup>189</sup>, R<sup>190</sup>, R<sup>191</sup>, R<sup>192</sup>, R<sup>193</sup>, R<sup>194</sup>, R<sup>195</sup>, R<sup>196</sup>, R<sup>197</sup>, R<sup>198</sup>, R<sup>199</sup>, R<sup>200</sup>, R<sup>201</sup>, and R<sup>202</sup>, independently of each other are a **hydrogen** atom (-H), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

or wherein the group PM

has the formula (IV)



- wherein R<sup>211</sup> and R<sup>212</sup>, independently of each other, are
- a **hydrogen** atom (-H); or an C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub> and C<sub>9</sub> branched or straight chain **alkyl**, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub> and C<sub>9</sub> branched or straight chain

**alkenyl**, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub> and C<sub>9</sub> branched or straight chain **alkinyl**, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub> and C<sub>9</sub> **cycloalkyl**, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub> and C<sub>9</sub> **cycloalkenyl**, **aryl**, **heteroaryl** or an **amino** group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted **amino** group (-NHR<sup>240</sup>; -NR<sup>241</sup>R<sup>242</sup>); and

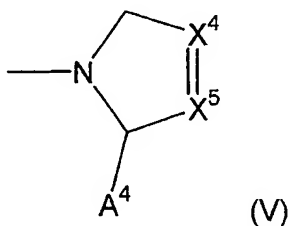
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the pairs R<sup>226</sup>/R<sup>227</sup>, R<sup>230</sup>/R<sup>231</sup>, R<sup>234</sup>/R<sup>235</sup>, R<sup>236</sup>/R<sup>237</sup> and R<sup>241</sup>/R<sup>242</sup>, independently of each other, may form a part of a **ring**; and
- wherein the substituents R<sup>220</sup>, R<sup>221</sup>, R<sup>222</sup>, R<sup>223</sup>, R<sup>224</sup>, R<sup>225</sup>, R<sup>226</sup>, R<sup>227</sup>, R<sup>228</sup>, R<sup>229</sup>, R<sup>230</sup>, R<sup>231</sup>, R<sup>232</sup>, R<sup>233</sup>, R<sup>234</sup>, R<sup>235</sup>, R<sup>236</sup>, R<sup>237</sup>, R<sup>238</sup>, R<sup>239</sup>, R<sup>240</sup>, R<sup>241</sup>, and R<sup>242</sup>, independently of each other, are a **hydrogen** atom (-H), or a C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub> and C<sub>9</sub> branched or straight chain **alkyl**, **aryl**, **heteroaryl**, **amino**, **halo**, **carbonyl**, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub> and C<sub>9</sub> branched or straight chain **alkoxy**, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub> and C<sub>9</sub> branched or straight chain **alkenoxy**, **phenyloxy**, **benzyloxy**, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub> and C<sub>9</sub> **cycloalkyl**, **cyano**, **amido**, **thiol**, **trifluoromethyl**, or **hydroxy** group; and
- wherein A<sup>3</sup> is
- a **hydrogen** atom (-H); or a **carbaldehyde** (-CHO), a **ketone** group (-CO-R<sup>260</sup>), a **boronic acid** group (-B(OH)<sub>2</sub>), a **cyano** group (-C≡N), a **carboxylic acid** group (-COOH), a **carboxylic acid ester** group (-COOR<sup>261</sup>), a **carboxylic acid anhydride** group (-CO-O-CO-R<sup>262</sup>), a **hydroxamic acid** group (-CO-NH(OH)), a N-substituted **hydroxamic acid** group (-CO-NR<sup>263</sup>(OH)), a O-substituted **hydroxamic acid** group (-CO-NH(OR<sup>264</sup>)), a **carboxamide** group (-CO-NH<sub>2</sub>), a N-substituted or N,N-disubstituted **carboxylic acid amide** group, (-CO-NHR<sup>265</sup>; -CO-NR<sup>266</sup>R<sup>267</sup>), an **amido** group (-HN-CO-R<sup>268</sup>), a **sulfonic acid** group (-SO<sub>3</sub>H), a **sulfonamide** group (-SO<sub>2</sub>-NH<sub>2</sub>), a N-substituted or N,N-disubstituted **sulfonamide** group (-SO<sub>2</sub>-NHR<sup>269</sup>; -SO<sub>2</sub>-NR<sup>270</sup>R<sup>271</sup>), an **amidosulfone** group (-NH-SO<sub>2</sub>-R<sup>272</sup>), a **sulfone** group (-SO<sub>2</sub>-R<sup>273</sup>), a **phosphoric acid** group

(-OP(=O)(OH)<sub>2</sub>), a **phosphoric acid ester** group (-OP(=O)(OR<sup>274</sup>)(OR<sup>275</sup>)), a **phosphonic acid** group (-P(=O)(OH)<sub>2</sub>), an **phosphonic acid ester** group (-P(=O)(OR<sup>276</sup>)(OR<sup>277</sup>)), a **halogen atom**, a **trifluormethyl** group (-CF<sub>3</sub>), a **thiol** group (-SH); a **thioether** group (-S-R<sup>278</sup>), a **hydroxy** group (-OH); an **alkoxy** group (-O-R<sup>279</sup>), a **tetrazole** group, an **amino** group (-NH<sub>2</sub>), or a **N-substituted** or **N,N-disubstituted amino** group (-NHR<sup>280</sup>; -NR<sup>281</sup>R<sup>282</sup>); and

- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; and,
- wherein optionally, the pairs R<sup>266</sup>/R<sup>267</sup>, R<sup>270</sup>/R<sup>271</sup>, R<sup>274</sup>/R<sup>275</sup>, R<sup>276</sup>/R<sup>277</sup> and R<sup>281</sup>/R<sup>282</sup>, independently of each other, may form a part of a **ring**; and
- wherein the substituents R<sup>260</sup>, R<sup>261</sup>, R<sup>262</sup>, R<sup>263</sup>, R<sup>264</sup>, R<sup>265</sup>, R<sup>266</sup>, R<sup>267</sup>, R<sup>268</sup>, R<sup>269</sup>, R<sup>270</sup>, R<sup>271</sup>, R<sup>272</sup>, R<sup>273</sup>, R<sup>274</sup>, R<sup>275</sup>, R<sup>276</sup>, R<sup>277</sup>, R<sup>278</sup>, R<sup>279</sup>, R<sup>280</sup>, R<sup>281</sup>, and R<sup>282</sup>, independently of each other are a **hydrogen atom** (-H), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

or wherein the group **PM**

has the formula (V)



- wherein X<sup>4</sup> is CR<sup>291</sup> or N; and

- wherein  $X^5$  is  $CR^{292}$  or N; and
- wherein  $R^{291}$  and  $R^{292}$ , independently of each other, are
  - a **hydrogen** atom (-H); or an  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkenyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkinyl**,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  **cycloalkyl**,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  **cycloalkenyl**, **aryl**, **heteroaryl** group, or an **amino** group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted **amino** group (-NHR<sup>320</sup>; -NR<sup>321</sup>R<sup>322</sup>); and
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the **the pair**  $R^{291}/R^{292}$ , if present, as well the pairs  $R^{306}/R^{307}$ ,  $R^{310}/R^{311}$ ,  $R^{314}/R^{315}$ ,  $R^{316}/R^{317}$  and  $R^{321}/R^{322}$ , independently of each other, may form a part of a **ring**; and
  - wherein the substituents  $R^{300}$ ,  $R^{301}$ ,  $R^{302}$ ,  $R^{303}$ ,  $R^{304}$ ,  $R^{305}$ ,  $R^{306}$ ,  $R^{307}$ ,  $R^{308}$ ,  $R^{309}$ ,  $R^{310}$ ,  $R^{311}$ ,  $R^{312}$ ,  $R^{313}$ ,  $R^{314}$ ,  $R^{315}$ ,  $R^{316}$ ,  $R^{317}$ ,  $R^{318}$ ,  $R^{319}$ ,  $R^{320}$ ,  $R^{321}$ , and  $R^{322}$ , independently of each other are a **hydrogen** atom (-H), or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkyl**, **aryl**, **heteroaryl**, **amino**, **halo**, **carbonyl**,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkoxy**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkenoxy**, **phenyloxy**, **benzyloxy**,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  **cycloalkyl**, **cyano**, **amido**, **thiol**, **trifluoromethyl**, or **hydroxy** group; and
- wherein  $A^4$  is
  - a **hydrogen** atom (-H); or a **carbaldehyde** (-CHO), a **ketone** group (-CO-R<sup>340</sup>), a **boronic acid** group (-B(OH)<sub>2</sub>), a **cyano** group (-C≡N), a **carboxylic acid** group (-COOH), a **carboxylic acid ester** group (-COOR<sup>341</sup>), a **carboxylic acid anhydride** group (-CO-O-CO-R<sup>342</sup>), a **hydroxamic acid** group (-CO-NH(OH)), a N-substituted **hydroxamic acid** group (-CO-NR<sup>343</sup>(OH)), a O-substituted **hydroxamic acid** group (-CO-NH(OR<sup>344</sup>)), a **carboxamide** group (-CO-NH<sub>2</sub>), a

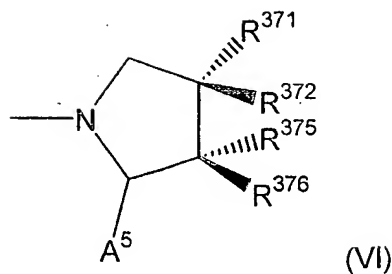
N-substituted or N,N-disubstituted **carboxylic acid amide** group,  $(-\text{CO}-\text{NHR}^{345}, -\text{CO}-\text{NR}^{346}\text{R}^{347})$ , an **amido group**  $(-\text{HN}-\text{CO}-\text{R}^{348})$ , a **sulfonic acid** group  $(-\text{SO}_3\text{H})$ , a **sulfonamide** group  $(-\text{SO}_2-\text{NH}_2)$ , a N-substituted or N,N-disubstituted **sulfonamide** group  $(-\text{SO}_2-\text{NHR}^{349}, -\text{SO}_2-\text{NR}^{350}\text{R}^{351})$ , an **amidosulfone** group  $(-\text{NH}-\text{SO}_2-\text{R}^{352})$ , a **sulfone** group  $(-\text{SO}_2-\text{R}^{353})$ , a **phosphoric acid** group  $(-\text{OP}(=\text{O})(\text{OH})_2)$ , a **phosphoric acid ester** group  $(-\text{OP}(=\text{O})(\text{OR}^{354})(\text{OR}^{355}))$ , a **phosphonic acid** group  $(-\text{P}(=\text{O})(\text{OH})_2)$ , an **phosphonic acid ester** group  $(-\text{P}(=\text{O})(\text{OR}^{356})(\text{OR}^{357}))$ , a **halogen atom**, a **trifluormethyl** group  $(-\text{CF}_3)$ , a **thiol** group  $(-\text{SH})$ ; a **thioether** group  $(-\text{S}-\text{R}^{358})$ , a **hydroxy** group  $(-\text{OH})$ ; an **alkoxy** group  $(-\text{O}-\text{R}^{359})$ , a **tetrazole** group, an **amino** group  $(-\text{NH}_2)$ , or a N-substituted or N,N-disubstituted **amino** group  $(-\text{NHR}^{360}, -\text{NR}^{361}\text{R}^{362})$ ; and

- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the pairs  $\text{R}^{346}/\text{R}^{347}$ ,  $\text{R}^{350}/\text{R}^{351}$ ,  $\text{R}^{354}/\text{R}^{355}$ ,  $\text{R}^{356}/\text{R}^{357}$  and  $\text{R}^{361}/\text{R}^{362}$ , independently of each other, may form a part of a **ring**; and
- wherein the substituents  $\text{R}^{340}, \text{R}^{341}, \text{R}^{342}, \text{R}^{343}, \text{R}^{344}, \text{R}^{345}, \text{R}^{346}, \text{R}^{347}, \text{R}^{348}, \text{R}^{349}, \text{R}^{350}, \text{R}^{351}, \text{R}^{352}, \text{R}^{353}, \text{R}^{354}, \text{R}^{355}, \text{R}^{356}, \text{R}^{357}, \text{R}^{358}, \text{R}^{359}, \text{R}^{360}, \text{R}^{361}$ , and  $\text{R}^{362}$ , independently of each other are a **hydrogen atom**  $(-\text{H})$ , or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

or wherein the group PM

has the formula (VI)

399



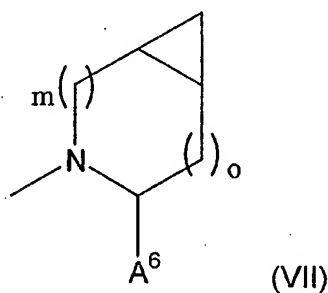
- wherein  $R^{371}$ ,  $R^{372}$ ,  $R^{375}$  and  $R^{376}$ , independently of each other, a **hydrogen** atom (-H); or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkenyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkinyl**,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  **cycloalkyl**,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  **cycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group or, a **carbaldehyde** (-CHO), a **ketone** group (-CO- $R^{380}$ ), a **boronic acid** group (-B(OH)<sub>2</sub>), a **cyano** group (-C≡N), a **carboxylic acid** group (-COOH), a **carboxylic acid ester** group (-COOR<sup>381</sup>), a **halogen atom**, a **trifluormethyl** group (-CF<sub>3</sub>), a **thiol** group (-SH); a **thioether** group (-S- $R^{398}$ ), a **hydroxy** group (-OH); an **alkoxy** group (-O- $R^{399}$ ), a **tetrazole** group, an **amino** group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted **amino** group (-NHR<sup>400</sup>; -NR<sup>401</sup>R<sup>402</sup>); and
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, any **two of the groups**  $R^{371}$ ,  $R^{372}$ ,  $R^{375}$ , and  $R^{376}$ , as well as the pairs  $R^{386}/R^{387}$ ,  $R^{390}/R^{391}$ ,  $R^{394}/R^{395}$ ,  $R^{396}/R^{397}$  and  $R^{401}/R^{402}$ , independently of each other, may form a part of a **ring**; and
- wherein the substituents  $R^{380}$ ,  $R^{381}$ ,  $R^{382}$ ,  $R^{383}$ ,  $R^{384}$ ,  $R^{385}$ ,  $R^{386}$ ,  $R^{387}$ ,  $R^{388}$ ,  $R^{389}$ ,  $R^{390}$ ,  $R^{391}$ ,  $R^{392}$ ,  $R^{393}$ ,  $R^{394}$ ,  $R^{395}$ ,  $R^{396}$ ,  $R^{397}$ ,  $R^{398}$ ,  $R^{399}$ ,  $R^{400}$ ,  $R^{401}$ , and

- $R^{402}$ , independently of each other are a **hydrogen atom (-H)**, or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkyl, aryl, heteroaryl, amino, halo, carbonyl**,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkoxy**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkenoxy, phenyloxy, benzyloxy**,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  **cycloalkyl, cyano, amido, thiol, trifluoromethyl, or hydroxy group**; and
- alternatively; the two groups  $R^{371}$  and  $R^{372}$  can be together an **oxo (=O)** or **hydroxyimino (=N-OH)** group; and
  - alternatively; the two groups  $R^{375}$  and  $R^{376}$  can be together an **oxo (=O)** or **hydroxyimino (=N-OH)** group; and
  - wherein  $A^5$  is
  - a **hydrogen atom (-H)**; or a **carbaldehyde (-CHO)**, a **ketone group (-CO- $R^{420}$ )**, a **boronic acid group (-B(OH)<sub>2</sub>)**, a **cyano group (-C≡N)**, a **carboxylic acid group (-COOH)**, a **carboxylic acid ester group (-COOR<sup>421</sup>)**, a **carboxylic acid anhydride group (-CO-O-CO- $R^{422}$ )**, a **hydroxamic acid group (-CO-NH(OH))**, a **N-substituted hydroxamic acid group (-CO-NR<sup>423</sup>(OH))**, a **O-substituted hydroxamic acid group (-CO-NH(OR<sup>424</sup>))**, a **carboxamide group (-CO-NH<sub>2</sub>)**, a **N-substituted or N,N-disubstituted carboxylic acid amide group, (-CO-NHR<sup>425</sup>, -CO-NR<sup>426</sup>R<sup>427</sup>)**, an **amido group (-HN-CO- $R^{428}$ )**, a **sulfonic acid group (-SO<sub>3</sub>H)**, a **sulfonamide group (-SO<sub>2</sub>-NH<sub>2</sub>)**, a **N-substituted or N,N-disubstituted sulfonamide group (-SO<sub>2</sub>-NHR<sup>429</sup>, -SO<sub>2</sub>-NR<sup>430</sup>R<sup>431</sup>)**, an **amidosulfone group (-NH-SO<sub>2</sub>-R<sup>432</sup>)**, a **sulfone group (-SO<sub>2</sub>-R<sup>433</sup>)**, a **phosphoric acid group (-OP(=O)(OH)<sub>2</sub>)**, a **phosphoric acid ester group (-OP(=O)(OR<sup>434</sup>)(OR<sup>435</sup>))**, a **phosphonic acid group (-P(=O)(OH)<sub>2</sub>)**, an **phosphonic acid ester group (-P(=O)(OR<sup>436</sup>)(OR<sup>437</sup>))**, a **halogen atom**, a **trifluormethyl group (-CF<sub>3</sub>)**, a **thiol group (-SH)**; a **thioether group (-S-R<sup>438</sup>)**, a **hydroxy group (-OH)**; an **alkoxy group (-O-R<sup>439</sup>)**, a **tetrazole group**, an **amino group (-NH<sub>2</sub>)**, or a **N-substituted or N,N-disubstituted amino group (-NHR<sup>440</sup>, -NR<sup>441</sup>R<sup>442</sup>)**; and

- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the pairs  $R^{426}/R^{427}$ ,  $R^{430}/R^{431}$ ,  $R^{434}/R^{435}$ ,  $R^{436}/R^{437}$  and  $R^{441}/R^{442}$ , independently of each other, may form a part of a **ring**; and
- wherein the substituents  $R^{420}$ ,  $R^{421}$ ,  $R^{422}$ ,  $R^{423}$ ,  $R^{424}$ ,  $R^{425}$ ,  $R^{426}$ ,  $R^{427}$ ,  $R^{428}$ ,  $R^{429}$ ,  $R^{430}$ ,  $R^{431}$ ,  $R^{432}$ ,  $R^{433}$ ,  $R^{434}$ ,  $R^{435}$ ,  $R^{436}$ ,  $R^{437}$ ,  $R^{438}$ ,  $R^{439}$ ,  $R^{440}$ ,  $R^{441}$ , and  $R^{442}$ , independently of each other are a **hydrogen atom (-H)**, or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

or wherein the group **PM**

has the formula (VII)



- wherein  $m$  is equal to 1 or 2, and  $o$  is equal to 1 or 2, and  $m$  or  $o$  can be 0;
- wherein  $A^6$  is a **hydrogen atom (-H)**; or a **carbaldehyde (-CHO)**, a **ketone** group ( $-\text{CO}-R^{460}$ ), a **boronic acid** group ( $-\text{B}(\text{OH})_2$ ), a **cyano** group ( $-\text{C}\equiv\text{N}$ ), a **carboxylic acid** group ( $-\text{COOH}$ ), a **carboxylic acid ester** group ( $-\text{COOR}^{461}$ ), a **carboxylic acid anhydride** group ( $-\text{CO}-\text{O}-\text{CO}-R^{462}$ ), a **hydroxamic acid** group

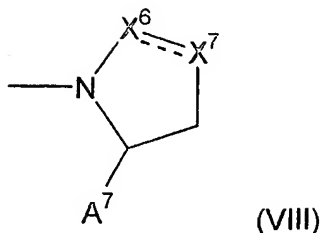


(-CO-NH(OH)), a N-substituted **hydroxamic acid** group (-CO-NR<sup>463</sup>(OH)), a O-substituted **hydroxamic acid** group (-CO-NH(OR<sup>464</sup>)), a **carboxamide** group (-CO-NH<sub>2</sub>), a N-substituted or N,N-disubstituted **carboxylic acid amide** group, (-CO-NHR<sup>465</sup>; -CO-NR<sup>466</sup>R<sup>467</sup>), an **amido group** (-HN-CO-R<sup>468</sup>), a **sulfonic acid** group (-SO<sub>3</sub>H), a **sulfonamide** group (-SO<sub>2</sub>-NH<sub>2</sub>), a N-substituted or N,N-disubstituted **sulfonamide** group (-SO<sub>2</sub>-NHR<sup>469</sup>; -SO<sub>2</sub>-NR<sup>470</sup>R<sup>471</sup>), an **amid sulfone** group (-NH-SO<sub>2</sub>-R<sup>472</sup>), a **sulfone** group (-SO<sub>2</sub>-R<sup>473</sup>), a **phosphoric acid** group (-OP(=O)(OH)<sub>2</sub>), a **phosphoric acid ester** group (-OP(=O)(OR<sup>474</sup>)(OR<sup>475</sup>)), a **phosphonic acid** group (-P(=O)(OH)<sub>2</sub>), an **phosphonic acid ester** group (-P(=O)(OR<sup>476</sup>)(OR<sup>477</sup>)), a **halogen atom**, a **trifluormethyl** group (-CF<sub>3</sub>), a **thiol** group (-SH); a **thioether** group (-S-R<sup>478</sup>), a **hydroxy** group (-OH); an **alkoxy** group (-O-R<sup>479</sup>), a **tetrazole** group, an **amino** group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted **amino** group (-NHR<sup>480</sup>; -NR<sup>481</sup>R<sup>482</sup>);

- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; and,
- wherein optionally, the pairs R<sup>466</sup>/R<sup>467</sup>, R<sup>470</sup>/R<sup>471</sup>, R<sup>474</sup>/R<sup>475</sup>, R<sup>476</sup>/R<sup>477</sup> and R<sup>481</sup>/R<sup>482</sup>, independently of each other, may form a part of a ring; and
- wherein the substituents R<sup>460</sup>, R<sup>461</sup>, R<sup>462</sup>, R<sup>463</sup>, R<sup>464</sup>, R<sup>465</sup>, R<sup>466</sup>, R<sup>467</sup>, R<sup>468</sup>, R<sup>469</sup>, R<sup>470</sup>, R<sup>471</sup>, R<sup>472</sup>, R<sup>473</sup>, R<sup>474</sup>, R<sup>475</sup>, R<sup>476</sup>, R<sup>477</sup>, R<sup>478</sup>, R<sup>479</sup>, R<sup>480</sup>, R<sup>481</sup>, and R<sup>482</sup>, independently of each other are a **hydrogen atom** (-H), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

or wherein the group PM

has the formula (VIII)



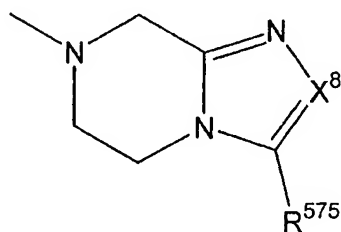
- wherein  $X^6$  is selected from  $CR^{490}R^{491}$ , O, S or  $NR^{492}$ , when the bond between  $X^6$  and  $X^7$  is a single bond; and
- wherein  $X^7$  is selected from  $CR^{493}R^{494}$ , O, S, or  $NR^{495}$ , when the bond between  $X^6$  and  $X^7$  is a single bond;
- **or alternatively,**
- wherein  $X^6$  is selected from  $CR^{496}$  or N, when the bond between  $X^6$  and  $X^7$  is a double bond; and
- wherein  $X^7$  is selected from  $CR^{497}$  or N, when the bond between  $X^6$  and  $X^7$  is a double bond; and
- wherein  $R^{490}$ ,  $R^{491}$ ,  $R^{492}$ ,  $R^{493}$ ,  $R^{494}$ ,  $R^{495}$ ,  $R^{496}$ , and  $R^{497}$ , independently of each other, are a **hydrogen** atom (-H); or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkenyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  branched or straight chain **alkinyl**,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  **cycloalkyl**,  $C_5$ ,  $C_6$ ,  $C_7$ ,  $C_8$  and  $C_9$  **cycloalkenyl**, **heteroalkyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group or, a **tetrazole** group, an **amino** group ( $-NH_2$ ), or a N-substituted or N,N-disubstituted **amino** group ( $-NHR^{520}$ ;  $-NR^{521}R^{522}$ ); and
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and,**

- wherein optionally, any two the groups  $R^{490}$ ,  $R^{491}$ ,  $R^{492}$ ,  $R^{493}$ ,  $R^{494}$ ,  $R^{495}$ ,  $R^{496}$ , and  $R^{497}$ , if present, as well as the pairs  $R^{506}/R^{507}$ ,  $R^{510}/R^{511}$ ,  $R^{514}/R^{515}$ ,  $R^{516}/R^{517}$  and  $R^{521}/R^{522}$ , independently of each other, may form a part of a **ring**; and
- wherein the substituents  $R^{500}$ ,  $R^{501}$ ,  $R^{502}$ ,  $R^{503}$ ,  $R^{504}$ ,  $R^{505}$ ,  $R^{506}$ ,  $R^{507}$ ,  $R^{508}$ ,  $R^{509}$ ,  $R^{510}$ ,  $R^{511}$ ,  $R^{512}$ ,  $R^{513}$ ,  $R^{514}$ ,  $R^{515}$ ,  $R^{516}$ ,  $R^{517}$ ,  $R^{518}$ ,  $R^{519}$ ,  $R^{520}$ ,  $R^{521}$ , and  $R^{522}$ , independently of each other are a **hydrogen atom** (-H), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group; and
- wherein  $A^7$  is
- a **hydrogen atom** (-H); or a **carbaldehyde** (-CHO), a **ketone group** (-CO- $R^{540}$ ), a **boronic acid group** (-B(OH)<sub>2</sub>), a **cyano group** (-C≡N), a **carboxylic acid group** (-COOH), a **carboxylic acid ester group** (-COOR<sup>541</sup>), a **carboxylic acid anhydride group** (-CO-O-CO- $R^{542}$ ), a **hydroxamic acid group** (-CO-NH(OH)), a **N-substituted hydroxamic acid group** (-CO-NR<sup>543</sup>(OH)), a **O-substituted hydroxamic acid group** (-CO-NH(OR<sup>544</sup>)), a **carboxamide group** (-CO-NH<sub>2</sub>), a **N-substituted or N,N-disubstituted carboxylic acid amide group**, (-CO-NHR<sup>545</sup>, -CO-NR<sup>546</sup>R<sup>547</sup>), an **amido group** (-HN-CO- $R^{548}$ ), a **sulfonic acid group** (-SO<sub>3</sub>H), a **sulfonamide group** (-SO<sub>2</sub>-NH<sub>2</sub>), a **N-substituted or N,N-disubstituted sulfonamide group** (-SO<sub>2</sub>-NHR<sup>549</sup>, -SO<sub>2</sub>-NR<sup>550</sup>R<sup>551</sup>), an **amidosulfone group** (-NH-SO<sub>2</sub>- $R^{552}$ ), a **sulfone group** (-SO<sub>2</sub>- $R^{553}$ ), a **phosphoric acid group** (-OP(=O)(OH)<sub>2</sub>), a **phosphoric acid ester group** (-OP(=O)(OR<sup>554</sup>)(OR<sup>555</sup>)), a **phosphonic acid group** (-P(=O)(OH)<sub>2</sub>), an **phosphonic acid ester group** (-P(=O)(OR<sup>556</sup>)(OR<sup>557</sup>)), a **halogen atom**, a **trifluormethyl group** (-CF<sub>3</sub>), a **thiol group** (-SH), a **thioether group** (-S- $R^{558}$ ), a **hydroxy group** (-OH), an **alkoxy group** (-O- $R^{559}$ ), a **tetrazole group**, an **amino group** (-NH<sub>2</sub>), or a **N-substituted or N,N-disubstituted amino group** (-NHR<sup>560</sup>, -NR<sup>561</sup>R<sup>562</sup>); and

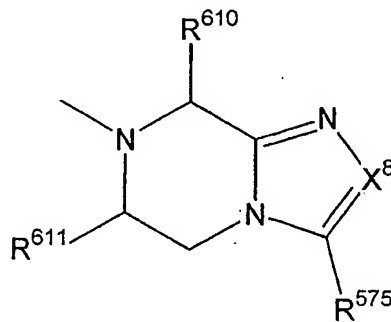
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the pairs  $R^{546}/R^{547}$ ,  $R^{550}/R^{551}$ ,  $R^{554}/R^{555}$ ,  $R^{556}/R^{557}$  and  $R^{561}/R^{562}$ , independently of each other, may form a part of a **ring**; and
- wherein the substituents  $R^{540}$ ,  $R^{541}$ ,  $R^{542}$ ,  $R^{543}$ ,  $R^{544}$ ,  $R^{545}$ ,  $R^{546}$ ,  $R^{547}$ ,  $R^{548}$ ,  $R^{549}$ ,  $R^{550}$ ,  $R^{551}$ ,  $R^{552}$ ,  $R^{553}$ ,  $R^{554}$ ,  $R^{555}$ ,  $R^{556}$ ,  $R^{557}$ ,  $R^{558}$ ,  $R^{559}$ ,  $R^{560}$ ,  $R^{561}$ , and  $R^{562}$ , independently of each other are a **hydrogen atom (-H)**, or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl group**;

or wherein the group PM

has the formula (IX) or (IXa)



(IX)



(IXa)

- wherein  $X^8$  is N or  $CR^{570}$ ; and
- wherein  $R^{570}$ ,  $R^{575}$ ,  $R^{610}$  and  $R^{611}$  independently of each other, are

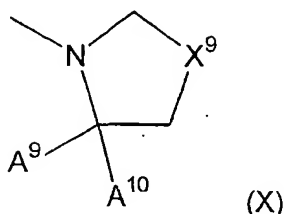
a **hydrogen atom** (-H); or an C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub> and C<sub>9</sub> branched or straight chain **alkyl**, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub> and C<sub>9</sub> branched or straight chain **alkenyl**, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub> and C<sub>9</sub> branched or straight chain **alkinyl**, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub> and C<sub>9</sub> **cycloalkyl**, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub> and C<sub>9</sub> **cycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **aryl-heteroalkyl** group or, a **carbaldehyde** (-CHO), a **ketone** group (-CO-R<sup>580</sup>), a **boronic acid** group (-B(OH)<sub>2</sub>), a **cyano** group (-C≡N), a **carboxylic acid** group (-COOH), a **carboxylic acid ester** group (-COOR<sup>581</sup>), a **carboxylic acid anhydride** group (-CO-O-CO-R<sup>582</sup>), a **hydroxamic acid** group (-CO-NH(OH)), a N-substituted **hydroxamic acid** group (-CO-NR<sup>583</sup>(OH)), a O-substituted **hydroxamic acid** group (-CO-NH(OR<sup>584</sup>)), a **carboxamide** group (-CO-NH<sub>2</sub>), a N-substituted or N,N-disubstituted **carboxylic acid amide** group, (-CO-NHR<sup>585</sup>; -CO-NR<sup>586</sup>R<sup>587</sup>), an **amido** group (-HN-CO-R<sup>588</sup>), a **sulfonic acid** group (-SO<sub>3</sub>H), a **sulfonamide** group (-SO<sub>2</sub>-NH<sub>2</sub>), a N-substituted or N,N-disubstituted **sulfonamide** group (-SO<sub>2</sub>-NHR<sup>589</sup>; -SO<sub>2</sub>-NR<sup>590</sup>R<sup>591</sup>), an **amidosulfone** group (-NH-SO<sub>2</sub>-R<sup>592</sup>), a **sulfone** group (-SO<sub>2</sub>-R<sup>593</sup>), a **phosphoric acid** group (-OP(=O)(OH)<sub>2</sub>), a **phosphoric acid ester** group (-OP(=O)(OR<sup>594</sup>)(OR<sup>595</sup>)), a **phosphonic acid** group (-P(=O)(OH)<sub>2</sub>), an **phosphonic acid ester** group (-P(=O)(OR<sup>596</sup>)(OR<sup>597</sup>)), a **halogen atom**, a **trifluormethyl** group (-CF<sub>3</sub>), a **thiol** group (-SH); a **thioether** group (-S-R<sup>598</sup>), a **hydroxy** group (-OH); an **alkoxy** group (-O-R<sup>599</sup>), a **tetrazole** group, an **amino** group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted **amino** group (-NHR<sup>600</sup>; -NR<sup>601</sup>R<sup>602</sup>);

- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the pairs R<sup>570</sup>/R<sup>575</sup>, if present, as well as the pairs R<sup>586</sup>/R<sup>587</sup>, R<sup>590</sup>/R<sup>591</sup>, R<sup>594</sup>/R<sup>595</sup>, R<sup>596</sup>/R<sup>597</sup> and R<sup>601</sup>/R<sup>602</sup>, independently of each other, may form a part of a **ring**; **and**
- wherein the substituents R<sup>580</sup>, R<sup>581</sup>, R<sup>582</sup>, R<sup>583</sup>, R<sup>584</sup>, R<sup>585</sup>, R<sup>586</sup>, R<sup>587</sup>, R<sup>588</sup>, R<sup>589</sup>, R<sup>590</sup>, R<sup>591</sup>, R<sup>592</sup>, R<sup>593</sup>, R<sup>594</sup>, R<sup>595</sup>, R<sup>596</sup>, R<sup>597</sup>, R<sup>598</sup>, R<sup>599</sup>, R<sup>600</sup>, R<sup>601</sup>, and

$R^{602}$ , independently of each other are a hydrogen atom (-H), or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group;

or wherein the group PM

has the formula (X)



- wherein the groups  $X^9$  is  $CR^{900}R^{901}$ , S, SO, SO<sub>2</sub> or  $NR^{902}$ 
  - wherein  $R^{900}$ ,  $R^{901}$  and  $R^{902}$ , are, independently of each other, selected from hydrogen, fluorine, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens, or  $-C(=O)NR^{910}R^{911}$ .
- wherein  $A^9$  and  $A^{10}$  are, independently of each other, selected from hydrogen, cyano,  $-C(=O)NR^{912}R^{913}$ , or C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein

- $R^{910}$  and  $R^{912}$ , are, independently of each other, selected from hydrogen, or C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens; and

- $R^{911}$  and  $R^{913}$ , are, independently of each other, selected from the group consisting of

(1) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5, substituents independently selected from halogen and  $R^{920}$ ;

(2)  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6 or 7 substituents independently selected from (a) 0, 1, 2, 3, 4, or 5 halogens, and (b) 0, 1, 2 substituents selected from the group consisting of

- (a) hydroxy,
- (b)  $-COOH$ ,
- (c)  $-COO(C_1, C_2, C_3, C_4, C_5 \text{ or } C_6 \text{ alkyl})$ , i.e. ester,
- (d) phenyl;
- (e) naphthyl,
- (f)  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  cycloalkyl,
- (g) a 5 - or 6 membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur;
- (h) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (a) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (b) a benzene ring fused to a 5- or 6-membered heterocycle having 1, 2, or 3 hetero atoms;

- wherein said  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  cycloalkyl, phenyl, naphthyl, are optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from halogen and  $R^{920}$ , and said 5 or 6 membered heterocycle and said 8, 9 or 10 - membered bicyclic ring system are each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, and  $R^{920}$ ; and

(3) C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl, which is optionally substituted with 1, 2, or 3 groups independently selected from halogen, hydroxy, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein R<sup>920</sup> is selected from the group consisting of:

- (1) hydroxy;
- (2) cyano;
- (3) C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl optionally substituted with 1, 2, or 3 groups independently selected from halogen, hydroxy, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, wherein said -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl are linear or branched and are optionally substituted with 1, 2, 3, 4, 5 or 6 substituents selected from 1, 2, 3, 4, or 5 halogens, and 0 or 1 substituents selected from -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, -COOH, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl substituents being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;
- (4) C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub>, C<sub>9</sub> or C<sub>10</sub> alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6, or 7 substituents independently selected from 0, 1, 2, 3, 4, or 5 halogen atoms and 0, 1, or 2 groups selected from
  - (a) hydroxy;
  - (b) -COOH;
  - (c) -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, which may linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens;
  - (d) a 5 - or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, optionally substituted with 1, 2, or 3



substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.;

(e) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (i) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (ii) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(f) -CONR<sup>925</sup>R<sup>925</sup>;

(g) -SO<sub>2</sub>NR<sup>925</sup>R<sup>925</sup>;

(h) -NR<sup>925</sup>-C(=O)R<sup>925</sup>

(i) -NR<sup>925</sup>-C(=O)NR<sup>925</sup>R<sup>925</sup>;

(j) -NR<sup>925</sup>COOR<sup>930</sup>

(k) -O-CO-R<sup>930</sup>

(l) -O-CO-NR<sup>925</sup>R<sup>925</sup>;

(m) -NR<sup>925</sup>SO<sub>2</sub>R<sup>930</sup>;

(n) -NR<sup>925</sup>R<sup>925</sup>;

(o) phenyl which is optionally substituted with 1, 2, 3, 4, or 5 group independently selected from halogen, hydroxy, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester being linear or branched and optionally substituted

with 1, 2, 3, 4, 5, or 6 substituents independently selected from 0 or 1 C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl and 0, 1, 2, 3, 4, or 5 halogens, and

(p) C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, which is optionally substituted with 1, 2, 3, 4, 5, or 6 halogens;

(5) OC<sub>1</sub>, OC<sub>2</sub>, OC<sub>3</sub>, OC<sub>4</sub>, OC<sub>5</sub>, OC<sub>6</sub>, OC<sub>7</sub>, OC<sub>8</sub>, OC<sub>9</sub> or OC<sub>10</sub> alkyl, which is linear or branched and is optionally substituted with 0, 1, 2, 3, 4, or 5 halogen atoms and 0, 1, or 2 substituents selected from

(a) hydroxy;

(b)-COOH;

(c) -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, which may be linear or branched and is optionally substituted with 1, 2, 3, 4 or 5 halogens;

(d) a 5 - or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.;

(e) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (i) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (ii) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(f) -CONR<sup>925</sup>R<sup>925</sup>;

(g)  $-\text{SO}_2\text{NR}^{925}\text{R}^{925}$ ;

(h)  $-\text{NR}^{925}-\text{C}(=\text{O})\text{R}^{925}$

(i)  $-\text{NR}^{925}-\text{C}(=\text{O})\text{NR}^{925}\text{R}^{925}$ ;

(j)  $-\text{NR}^{925}\text{COOR}^{930}$

(k)  $-\text{O}-\text{CO}-\text{R}^{930}$

(l)  $-\text{O}-\text{CO}-\text{NR}^{925}\text{R}^{925}$ ;

(m)  $-\text{NR}^{925}\text{SO}_2\text{R}^{930}$ ;

(n)  $-\text{NR}^{925}\text{R}^{925}$ ;

(o) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5 groups independently selected from halogen, hydroxy,  $\text{C}_1$ ,  $\text{C}_2$ ,  $\text{C}_3$ ,  $\text{C}_4$ ,  $\text{C}_5$  or  $\text{C}_6$  alkyl,  $-\text{OC}_1$ ,  $-\text{OC}_2$ ,  $-\text{OC}_3$ ,  $-\text{OC}_4$ ,  $-\text{OC}_5$  or  $-\text{OC}_6$  alkyl,  $-\text{COOH}$ ,  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester, said  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  alkyl,  $-\text{OC}_1$ ,  $-\text{OC}_2$ ,  $-\text{OC}_3$ ,  $-\text{OC}_4$ ,  $-\text{OC}_5$  or  $-\text{OC}_6$  alkyl,  $-\text{COOH}$ ,  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, 5, or 6 substituents independently selected from 0 or 1  $\text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  cycloalkyl and 0, 1, 2, 3, 4, or 5 halogens, and

(p)  $\text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  cycloalkyl, which is optionally substituted with 1, 2, 3, 4, 5, or 6 halogens;

(6)  $-\text{COOH}$ ;

(7)  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester, which may be linear or branched and is optionally substituted with 1, 2, 3, 4, 5 halogens;

(8) a 5 - or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, said heterocycle being optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen,  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5$  or  $-\text{OC}_6$  alkyl, said  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5$  or  $-\text{OC}_6$  alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.

(9) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (a) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen,

oxygen or sulfur, or (b) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(10) -CONR<sup>925</sup>R<sup>925</sup>;

(11) -SO<sub>2</sub>NR<sup>925</sup>R<sup>925</sup>;

(12) -NR<sup>925</sup>-C(=O)R<sup>925</sup>

(13) -NR<sup>925</sup>-C(=O)NR<sup>925</sup>R<sup>925</sup>;

(14) -NR<sup>925</sup>COOR<sup>930</sup>

(15) -O-CO-R<sup>930</sup>

(16) -O-CO-NR<sup>925</sup>R<sup>925</sup>;

(17) -NR<sup>925</sup>SO<sub>2</sub>R<sup>930</sup>;

(18) -NR<sup>925</sup>R<sup>925</sup>;

(19) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5 group independently selected from halogen, hydroxy, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

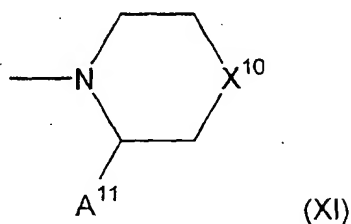
wherein R<sup>930</sup> is selected from the group consisting of phenyl, C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, and C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, wherein C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6, substituents independently selected from 0, 1, 2, 3, 4, or 5 halogens, 0 or 1 phenyl, wherein said optional phenyl substituent and said R<sup>930</sup>, when R<sup>930</sup> is phenyl or C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, are optionally substituted with 1, 2, 3, 4, or 5 substituents, independently selected from

halogen, OH, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, or C<sub>5</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, or -OC<sub>5</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, or C<sub>5</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, or -OC<sub>5</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.

wherein R<sup>925</sup> is selected from R<sup>930</sup> and hydrogen.

wherein the group PM

has the formula (XI)



- wherein the groups X<sup>10</sup> is CR<sup>1000</sup>R<sup>1001</sup>, S, SO, SO<sub>2</sub> or NR<sup>1002</sup>
  - wherein R<sup>1000</sup>, R<sup>1001</sup> and R<sup>1002</sup> are, independently of each other, selected from hydrogen, fluorine, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens, or -C(=O)NR<sup>1010</sup>R<sup>1011</sup>.

and A<sup>11</sup> is selected from

hydrogen, cyano, -C(=O)NR<sup>1012</sup>R<sup>1013</sup>, or C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein

- R<sup>1010</sup> and R<sup>1012</sup> are, independently of each other, selected from hydrogen, or C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens; and

- $R^{1011}$  and  $R^{1013}$ , are, independently of each other, selected from the group consisting of

(1) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5, substituents independently selected from halogen and  $R^{1020}$ ;

(2)  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6 or 7 substituents independently selected from (a) 0, 1, 2, 3, 4, or 5 halogens, and (b) 0, 1, 2 substituents selected from the group consisting of

- (a) hydroxy,
- (b)  $-COOH$ ,
- (c)  $-COO(C_1, C_2, C_3, C_4, C_5$  or  $C_6$  alkyl), i.e. ester,
- (d) phenyl,
- (e) naphthyl,
- (f)  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  cycloalkyl,
- (g) a 5 - or 6 membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur;
- (h) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (a) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (b) a benzene ring fused to a 5- or 6-membered heterocycle having 1, 2, or 3 hetero atoms;

- wherein said  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  cycloalkyl, phenyl, naphthyl, are optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from halogen and  $R^{1020}$ , and said 5 or 6 membered heterocycle and said 8, 9 or 10 - membered bicyclic ring system are each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, and  $R^{1020}$ ; and

(3) C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, which is optionally substituted with 1, 2, or 3 groups independently selected from halogen, hydroxy, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein R<sup>1020</sup> is selected from the group consisting of:

- (1) hydroxy;
- (2) cyano;
- (3) C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl optionally substituted with 1, 2, or 3 groups independently selected from halogen, hydroxy, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, wherein said -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl are linear or branched and are optionally substituted with 1, 2, 3, 4, 5 or 6 substituents selected from 1, 2, 3, 4, or 5 halogens, and 0 or 1 substituents selected from -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, -COOH, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl substituents being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;
- (4) C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub>, C<sub>9</sub> or C<sub>10</sub> alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6, or 7 substituents independently selected from 0, 1, 2, 3, 4, or 5 halogen atoms and 0, 1, or 2 groups selected from
  - (a) hydroxy;
  - (b) -COOH;
  - (c) -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, which may linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens;
  - (d) a 5 - or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, optionally substituted with 1, 2, or 3

substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.;

(e) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (i) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (ii) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(f) -CONR<sup>1025</sup>R<sup>1025</sup>;

(g) -SO<sub>2</sub>NR<sup>1025</sup>R<sup>1025</sup>;

(h) -NR<sup>1025</sup>-C(=O)R<sup>1025</sup>

(i) -NR<sup>1025</sup>-C(=O)NR<sup>1025</sup>R<sup>1025</sup>;

(j) -NR<sup>1025</sup>COOR<sup>1030</sup>

(k) -O-CO-R<sup>1030</sup>

(l) -O-CO-NR<sup>1025</sup>R<sup>1025</sup>;

(m) -NR<sup>1025</sup>SO<sub>2</sub>R<sup>1030</sup>;

(n) -NR<sup>1025</sup>R<sup>1025</sup>;

(o) phenyl which is optionally substituted with 1, 2, 3, 4, or 5 group independently selected from halogen, hydroxy, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester being linear or branched and optionally substituted



with 1, 2, 3, 4, 5, or 6 substituents independently selected from 0 or 1 C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl and 0, 1, 2, 3, 4, or 5 halogens, and

(p) C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl, which is optionally substituted with 1, 2, 3, 4, 5, or 6 halogens;

(5) OC<sub>1</sub>, OC<sub>2</sub>, OC<sub>3</sub>, OC<sub>4</sub>, OC<sub>5</sub>, OC<sub>6</sub>, OC<sub>7</sub>, OC<sub>8</sub>, OC<sub>9</sub> or OC<sub>10</sub> alkyl, which is linear or branched and is optionally substituted with 0, 1, 2, 3, 4, or 5 halogen atoms and 0, 1, or 2 substituents selected from

(a) hydroxy;

(b) -COOH;

(c) -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, which may be linear or branched and is optionally substituted with 1, 2, 3, 4 or 5 halogens;

(d) a 5 - or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.;

(e) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (i) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (ii) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(f) -CONR<sup>1025</sup>R<sup>1025</sup>;

(g)  $-\text{SO}_2\text{NR}^{1025}\text{R}^{1025}$ ,

(h)  $-\text{NR}^{1025}-\text{C}(=\text{O})\text{R}^{1025}$

(i)  $-\text{NR}^{1025}-\text{C}(=\text{O})\text{NR}^{1025}\text{R}^{1025}$ ,

(j)  $-\text{NR}^{1025}\text{COOR}^{1030}$

(k)  $-\text{O}-\text{CO}-\text{R}^{1030}$

(l)  $-\text{O}-\text{CO}-\text{NR}^{1025}\text{R}^{1025}$ ,

(m)  $-\text{NR}^{1025}\text{SO}_2\text{R}^{1030}$ ,

(n)  $-\text{NR}^{1025}\text{R}^{1025}$ ,

(o) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5 groups independently selected from halogen, hydroxy,  $\text{C}_1$ ,  $\text{C}_2$ ,  $\text{C}_3$ ,  $\text{C}_4$ ,  $\text{C}_5$  or  $\text{C}_6$  alkyl,  $-\text{OC}_1$ ,  $-\text{OC}_2$ ,  $-\text{OC}_3$ ,  $-\text{OC}_4$ ,  $-\text{OC}_5$  or  $-\text{OC}_6$  alkyl,  $-\text{COOH}$ ,  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester, said  $\text{C}_1$ ,  $\text{C}_2$ ,  $\text{C}_3$ ,  $\text{C}_4$ ,  $\text{C}_5$  or  $\text{C}_6$  alkyl,  $-\text{OC}_1$ ,  $-\text{OC}_2$ ,  $-\text{OC}_3$ ,  $-\text{OC}_4$ ,  $-\text{OC}_5$  or  $-\text{OC}_6$  alkyl,  $-\text{COOH}$ ,  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, 5, or 6 substituents independently selected from 0 or 1  $\text{C}_3$ ,  $\text{C}_4$ ,  $\text{C}_5$  or  $\text{C}_6$  cycloalkyl and 0, 1, 2, 3, 4, or 5 halogens, and

(p)  $\text{C}_3$ ,  $\text{C}_4$ ,  $\text{C}_5$  or  $\text{C}_6$  cycloalkyl, which is optionally substituted with 1, 2, 3, 4, 5, or 6 halogens;

(6)  $-\text{COOH}$ ;

(7)  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester, which may be linear or branched and is optionally substituted with 1, 2, 3, 4, 5 halogens;

(8) a 5- or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, said heterocycle being optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen,  $\text{C}_1$ ,  $\text{C}_2$ ,  $\text{C}_3$ ,  $\text{C}_4$ ,  $\text{C}_5$  or  $\text{C}_6$  alkyl, and  $-\text{OC}_1$ ,  $-\text{OC}_2$ ,  $-\text{OC}_3$ ,  $-\text{OC}_4$ ,  $-\text{OC}_5$  or  $-\text{OC}_6$  alkyl, said  $\text{C}_1$ ,  $\text{C}_2$ ,  $\text{C}_3$ ,  $\text{C}_4$ ,  $\text{C}_5$  or  $\text{C}_6$  alkyl, and  $-\text{OC}_1$ ,  $-\text{OC}_2$ ,  $-\text{OC}_3$ ,  $-\text{OC}_4$ ,  $-\text{OC}_5$  or  $-\text{OC}_6$  alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.

(9) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (a) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen,

oxygen or sulfur, or (b) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(10) -CONR<sup>1025</sup>R<sup>1025</sup>;

(11) -SO<sub>2</sub>NR<sup>1025</sup>R<sup>1025</sup>;

(12) -NR<sup>1025</sup>-C(=O)R<sup>1025</sup>

(13) -NR<sup>1025</sup>-C(=O)NR<sup>1025</sup>R<sup>1025</sup>;

(14) -NR<sup>925</sup>COOR<sup>1030</sup>

(15) -O-CO-R<sup>1030</sup>

(16) -O-CO-NR<sup>1025</sup>R<sup>1025</sup>;

(17) -NR<sup>1025</sup>SO<sub>2</sub>R<sup>1030</sup>;

(18) -NR<sup>1025</sup>R<sup>1025</sup>;

(19) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5 group independently selected from halogen, hydroxy, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

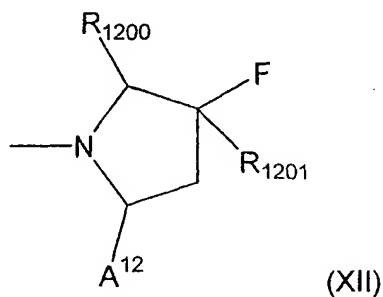
wherein R<sup>1030</sup> is selected from the group consisting of phenyl, C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, and C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, wherein C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6, substituents independently selected from 0, 1, 2, 3, 4, or 5 halogens, 0 or 1 phenyl, wherein said optional phenyl substituent and said R<sup>930</sup>, when R<sup>930</sup> is phenyl or C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, are optionally substituted with 1, 2, 3, 4, or 5 substituents, independently selected from

halogen, OH, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, or C<sub>5</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, or -OC<sub>5</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, or C<sub>5</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, or -OC<sub>5</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.

wherein R<sup>1025</sup> is selected from R<sup>1030</sup> and hydrogen.

or wherein the group PM

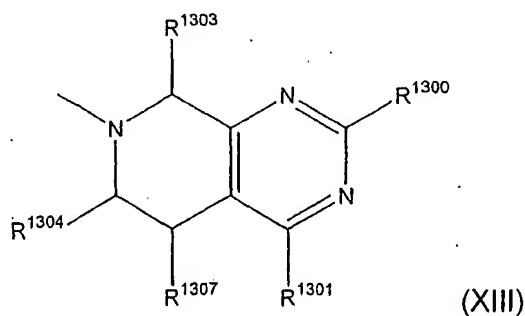
has the formula (XII)



- wherein the groups R<sup>1201</sup> is hydrogen or fluoro.
- wherein R<sup>1200</sup> and A<sup>12</sup> is selected from hydrogen and cyano, and the other is hydrogen.

or wherein the group PM

has the formula XIII:



wherein:

-  $R^{1300}$  and  $R^{1301}$  are independently selected from the group consisting of:

- (10) hydrogen,
- (11) CN,
- (12)  $C_{1-10}$ alkyl, which is linear or branched which is unsubstituted or substituted with:
  - a) halogen, or
  - b) phenyl, which is unsubstituted or substituted with 1 - 5 substituents independently selected from halogen, CN, OH,  $R^{1302}$ ,  $OR^{1302}$ ,  $NHSO_2R^{1302}$ ,  $N(C_{1-6}alkyl)SO_2R^{1302}$ ,  $SO_2R^{1302}$ ,  $SO_2NR^{1305}R^{1306}$ ,  $NR^{1305}R^{1306}$ ,  $CONR^{1305}R^{1306}$ ,  $CO_2H$ , and  $CO_2C_{1-6}alkyl$ , wherein the  $C_{1-6}alkyl$  is linear or branched,
- (13) phenyl which is unsubstituted or substituted with 1 - 5 substituents independently selected from halogen, CN, OH,  $R^{1302}$ ,  $OR^{1302}$ ,  $NHSO_2R^{1302}$ ,  $N(C_{1-6}alkyl)SO_2R^{1302}$ ,  $SO_2R^{1302}$ ,  $SO_2NR^{1305}R^{1306}$ ,  $NR^{1305}R^{1306}$ ,  $CONR^{1305}R^{1306}$ ,  $CO_2H$ , and  $CO_2C_{1-6}alkyl$ , wherein the  $C_{1-6}alkyl$  is linear or branched,
- (14) a 5- or 6-membered heterocyclic which may be saturated or unsaturated comprising 1 - 4 heteroatoms independently selected from N, S and O, the heterocycle being unsubstituted or substituted with 1 - 3 substituents independently selected from oxo, halogen,  $NO_2$ , CN, OH,  $R^{1302}$ ,  $OR^{1302}$ ,  $NHSO_2R^{1302}$ ,  $N(C_{1-6}alkyl)SO_2R^{1302}$ ,  $SO_2R^{1302}$ ,  $SO_2NR^{1305}R^{1306}$ ,  $NR^{1305}R^{1306}$ ,  $CONR^{1305}R^{1306}$ ,  $CO_2H$ , and  $CO_2C_{1-6}alkyl$ , wherein the  $C_{1-6}alkyl$  is linear or branched,
- (15)  $C_{3-6}$ cycloalkyl, which is optionally substituted with 1 - 5 substituents independently selected from halogen, OH,  $C_{1-6}alkyl$ , and  $OC_{1-6}alkyl$ , wherein the  $C_{1-6}alkyl$  and  $OC_{1-6}alkyl$  are linear or branched and optionally substituted with 1 - 5 halogens,
- (16) OH,
- (17)  $OR^{1302}$ , and

(18)  $\text{NR}^{1305}\text{R}^{1306}$

-  $\text{R}^{1302}$  is  $\text{C}_{1-6}$ alkyl, which is linear or branched and which is unsubstituted or substituted with 1 – 5 groups independently selected from halogen,  $\text{CO}_2\text{H}$ , and  $\text{CO}_2\text{C}_{1-6}$ alkyl, wherein the  $\text{C}_{1-6}$ alkyl is linear or branched;

-  $\text{R}^{1303}$  is selected from the group consisting of:

(10) hydrogen,

(11)  $\text{C}_{1-10}$ alkyl, which is linear or branched and which is unsubstituted or substituted with one or more substituted selected from:

a) halogen,

b) hydroxy,

c) phenyl, which is unsubstituted or substituted with 1 – 5 substituents independently selected from halogen, OH,  $\text{C}_{1-6}$ alkyl, and  $\text{OC}_{1-6}$ alkyl, wherein the  $\text{C}_{1-6}$ alkyl is linear or branched and optionally substituted with 1 – 5 halogens,

d) naphthyl, wherein the naphthyl is optionally substituted with 1 – 5 substituents independently selected from halogen, OH,  $\text{C}_{1-6}$ alkyl, and  $\text{OC}_{1-6}$ alkyl, wherein the  $\text{C}_{1-6}$ alkyl is linear or branched and optionally substituted with 1 – 5 halogens,

k)  $\text{CO}_2\text{H}$ ,

l)  $\text{CO}_2\text{C}_{1-6}$ alkyl,

m)  $\text{CONR}^{1305}\text{R}^{1306}$ ,

(12) CN,

(13) phenyl which is unsubstituted or substituted with 1 – 5 substituents independently selected from  $\text{C}_{1-6}$ alkyl, and  $\text{OC}_{1-6}$ alkyl, hydroxy and halogen, wherein the  $\text{C}_{1-6}$ alkyl is linear or branched and optionally substituted with 1 – 5 halogens

(14) naphthyl which is unsubstituted or substituted with 1 – 5 substituents independently selected from  $\text{C}_{1-6}$ alkyl, and  $\text{OC}_{1-6}$ alkyl, hydroxy and halogen,

wherein the C<sub>1-6</sub>alkyl is linear or branched and optionally substituted with 1 – 5 halogens,

- (15) CO<sub>2</sub>H,
- (16) CO<sub>2</sub>C<sub>1-6</sub>alkyl,
- (17) CONR<sup>1305</sup>R<sup>1306</sup>, and
- (18) C<sub>3-6</sub>cycloalkyl, which is unsubstituted or substituted with 1 – 5 substituents independently selected from C<sub>1-6</sub>alkyl, and OC<sub>1-6</sub>alkyl, hydroxy and halogen, wherein the C<sub>1-6</sub>alkyl is linear or branched and optionally substituted with 1 – 5 halogens

- R<sup>1305</sup> and R<sup>1306</sup> are independently selected from the group consisting of:

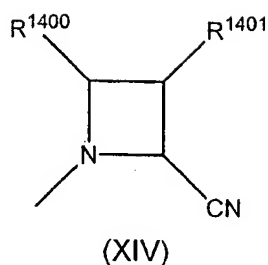
- (5) hydrogen,
- (6) phenyl, which is unsubstituted or substituted with substituents independently selected from halogen, OH, C<sub>1-6</sub>alkyl, and OC<sub>1-6</sub>alkyl, wherein the C<sub>1-6</sub>alkyl is linear or branched and optionally substituted with 1 – 5 halogens;
- (7) C<sub>3-6</sub>cycloalkyl, which is unsubstituted or substituted with 1 – 5 substituents independently selected from C<sub>1-6</sub>alkyl, and OC<sub>1-6</sub>alkyl, wherein the C<sub>1-6</sub>alkyl is linear or branched and optionally substituted with 1 – 5 halogens,
- (8) C<sub>1-6</sub>alkyl, which is linear or branched and which is unsubstituted or substituted with:
  - a) halogen, or
  - b) phenyl, which is unsubstituted or substituted with 1 – 5 substituents independently selected from halogen, OH, C<sub>1-6</sub>alkyl, and OC<sub>1-6</sub>alkyl, wherein the C<sub>1-6</sub>alkyl is linear or branched and optionally substituted with 1 – 5 halogens,

or wherein R<sup>1305</sup> and R<sup>1306</sup> together with the nitrogen atom to which they are attached form a heterocyclic ring selected from azetidine, pyrrolidine, piperidine, piperazine, and morpholine wherein said heterocyclic ring is unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, C<sub>1-6</sub>alkyl, and C<sub>1-6</sub>alkoxy, wherein alkyl and alkoxy are unsubstituted with one to five halogens;

-  $R^{1304}$  and  $R^{1307}$  are hydrogen;

or wherein the group PM

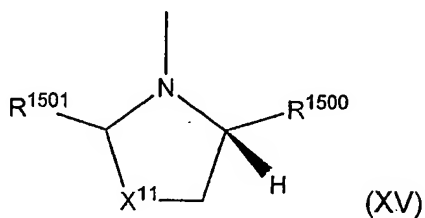
has the formula XIV:



- wherein  $R^{1400}$  and  $R^{1401}$ , independently of each other, are a **hydrogen** atom (-H); or halogen, cyano or ethynyl;

or wherein the group PM

has the formula XV:



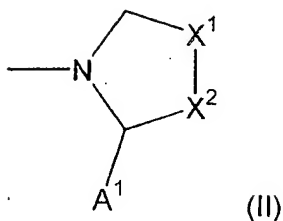
- wherein  $X^{11}$  is  $CH_2$ ,  $CHF$  or  $CF_2$ ;
- wherein  $R^{1500}$  is cyano;
- wherein  $R^{1501}$  is selected from the group consisting of alkoxyalkyl, alkyl, alkylcarbonyl, alkenyl, alkynyl, allenyl, arylalkyl, cycloalkyl, cycloalkylalkyl, cyano, haloalkyl, haloalkenyl, heterocyclealkyl, and hydroxyalkyl;



8. Compound according to claims 1, 2, 3, 4, 5, 6, and/or 7

wherein the group PM

has the formula (II)



- wherein  $X^1$  is  $CR^{51}R^{52}$ , O, S, or  $NR^{53}$ ; and
- wherein  $X^2$  is  $CR^{54}R^{55}$ , O, S, or  $NR^{56}$ ; and

wherein  $R^{51}$ ,  $R^{52}$ ,  $R^{53}$ ,  $R^{54}$ ,  $R^{55}$ , and  $R^{56}$ , independently of each other, are

- a **hydrogen** atom (-H); or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , and  $C_5$  branched or straight chain **alkyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkenyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkinyl**,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ , and  $C_7$  **cycloalkyl**, **aryl**, **heteroaryl** group or, an **amino** group ( $-NH_2$ ), or a N-substituted or N,N-disubstituted **amino** group ( $-NHR^{80}$ ;  $-NR^{81}R^{82}$ ); and
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, any **two of the groups**  $R^{51}$ ,  $R^{52}$ ,  $R^{53}$ ,  $R^{54}$ ,  $R^{55}$ , and  $R^{56}$ , if present, as well as the pairs  $R^{66}/R^{67}$ ,  $R^{70}/R^{71}$ ,  $R^{74}/R^{75}$ ,  $R^{76}/R^{77}$  and  $R^{81}/R^{82}$ , independently of each other, may form a part of a **ring**; and

- wherein the substituents  $R^{60}$ ,  $R^{61}$ ,  $R^{62}$ ,  $R^{63}$ ,  $R^{64}$ ,  $R^{65}$ ,  $R^{66}$ ,  $R^{67}$ ,  $R^{68}$ ,  $R^{69}$ ,  $R^{70}$ ,  $R^{71}$ ,  $R^{72}$ ,  $R^{73}$ ,  $R^{74}$ ,  $R^{75}$ ,  $R^{76}$ ,  $R^{77}$ ,  $R^{78}$ ,  $R^{79}$ ,  $R^{80}$ ,  $R^{81}$ , and  $R^{82}$ , independently of each other, are a **hydrogen atom** (-H), or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , and  $C_5$  branched or straight chain **alkyl**, **aryl**, **heteroaryl**, **amino**, **halo**, **carbonyl**,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkoxy**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  branched or straight chain **alkenoxy**, **phenoxy**, **benzyloxy**,  $C_3$ ,  $C_4$ ,  $C_5$  **cycloalkyl**, **cyano**, **amido**, **thiol** **trifluoromethyl**, or **hydroxy group**; and

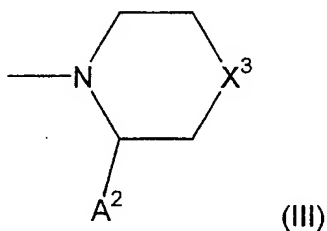
wherein  $A^1$  is

- a **hydrogen atom** (-H) or a **carbaldehyde** (-CHO), a **ketone group** (-CO- $R^{100}$ ), a **boronic acid group** (-B(OH)<sub>2</sub>), a **cyano group** (-C≡N), a **carboxylic acid group** (-COOH), a **carboxylic acid ester group** (-COOR<sup>101</sup>), a **carboxylic acid anhydride group** (-CO-O-CO- $R^{102}$ ), a **hydroxamic acid group** (-CO-NH(OH)), a **N-substituted hydroxamic acid group** (-CO-NR<sup>103</sup>(OH)), a **O-substituted hydroxamic acid group** (-CO-NH(OR<sup>104</sup>)), a **carboxamide group** (-CO-NH<sub>2</sub>), a **N-substituted or N,N-disubstituted carboxylic acid amide group**, (-CO-NHR<sup>105</sup>; -CO-NR<sup>106</sup>R<sup>107</sup>), an **amido group** (-HN-CO- $R^{108}$ ), a **sulfonic acid group** (-SO<sub>3</sub>H), a **sulfonamide group** (-SO<sub>2</sub>-NH<sub>2</sub>), a **N-substituted or N,N-disubstituted sulfonamide group** (-SO<sub>2</sub>-NHR<sup>109</sup>; -SO<sub>2</sub>-NR<sup>110</sup>R<sup>111</sup>), an **amid sulfone group** (-NH-SO<sub>2</sub>- $R^{112}$ ), a **sulfone group** (-SO<sub>2</sub>- $R^{113}$ ), a **phosphoric acid group** (-OP(=O)(OH)<sub>2</sub>), a **phosphoric acid ester group** (-OP(=O)(OR<sup>114</sup>)(OR<sup>115</sup>)), a **phosphonic acid group** (-P(=O)(OH)<sub>2</sub>), an **phosphonic acid ester group** (-P(=O)(OR<sup>116</sup>)(OR<sup>117</sup>)), a **halogen atom**, a **trifluoromethyl group** (-CF<sub>3</sub>), a **thiol group** (-SH); a **thioether group** (-S- $R^{118}$ ), a **hydroxy group** (-OH); an **alkoxy group** (-O- $R^{119}$ ), a **tetrazole group**, an **amino group** (-NH<sub>2</sub>), or a **N-substituted or N,N-disubstituted amino group** (-NHR<sup>120</sup>; -NR<sup>121</sup>R<sup>122</sup>); and wherein optionally, the pairs  $R^{106}/R^{107}$ ,  $R^{110}/R^{111}$ ,  $R^{114}/R^{115}$ ,  $R^{116}/R^{117}$  and  $R^{121}/R^{122}$ , independently of each other, may form a part of a **ring**; and
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; and,

- wherein the substituents  $R^{100}$ ,  $R^{101}$ ,  $R^{102}$ ,  $R^{103}$ ,  $R^{104}$ ,  $R^{105}$ ,  $R^{106}$ ,  $R^{107}$ ,  $R^{108}$ ,  $R^{109}$ ,  $R^{110}$ ,  $R^{111}$ ,  $R^{112}$ ,  $R^{113}$ ,  $R^{114}$ ,  $R^{115}$ ,  $R^{116}$ ,  $R^{117}$ ,  $R^{118}$ ,  $R^{119}$ ,  $R^{120}$ ,  $R^{121}$ , and  $R^{122}$ , independently of each other, are a **hydrogen atom (-H)**, or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

or wherein the group **PM**

has the formula (III)



- wherein  $X^3$  is  $CR^{131}R^{132}$ , O, S, or  $NR^{133}$ ; and
- wherein  $R^{131}$ ,  $R^{132}$ , and  $R^{133}$ , independently of each other, are
- a **hydrogen atom (-H)**; or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , and  $C_5$  branched or straight chain **alkyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkenyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkinyl**,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ , and  $C_7$  **cycloalkyl**, **aryl**, **heteroaryl** group or, an **amino** group ( $-NH_2$ ), or a **N-substituted** or **N,N-disubstituted amino** group ( $-NHR^{160}$ ,  $-NR^{161}R^{162}$ ); and
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the **the pair**  $R^{131}/R^{132}$ , if present, as well the pairs  $R^{146}/R^{147}$ ,  $R^{150}/R^{151}$ ,  $R^{154}/R^{155}$ ,  $R^{156}/R^{157}$  and  $R^{161}/R^{162}$ , independently of each other, may form a part of a **ring**; and

- wherein the substituents  $R^{140}$ ,  $R^{141}$ ,  $R^{142}$ ,  $R^{143}$ ,  $R^{144}$ ,  $R^{145}$ ,  $R^{146}$ ,  $R^{147}$ ,  $R^{148}$ ,  $R^{149}$ ,  $R^{150}$ ,  $R^{151}$ ,  $R^{152}$ ,  $R^{153}$ ,  $R^{154}$ ,  $R^{155}$ ,  $R^{156}$ ,  $R^{157}$ ,  $R^{158}$ ,  $R^{159}$ ,  $R^{160}$ ,  $R^{161}$ , and  $R^{162}$ , independently of each other are a **hydrogen atom** (-H), or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , and  $C_5$  branched or straight chain **alkyl**, **aryl**, **heteroaryl**, **amino**, **halo**, **carbonyl**,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkoxy**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  branched or straight chain **alkenoxy**, **phenyloxy**, **benzyloxy**,  $C_3$ ,  $C_4$ ,  $C_5$  **cycloalkyl**, **cyano**, **amido**, **thiol** **trifluoromethyl**, or **hydroxy** group; and

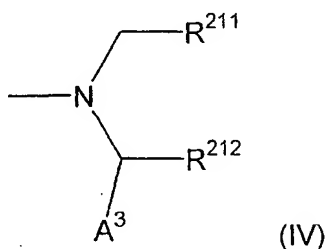
wherein  $A^2$  is

- a **hydrogen atom** (-H); or a **carbaldehyde** (-CHO), a **ketone** group (-CO- $R^{180}$ ), a **boronic acid** group (-B(OH)<sub>2</sub>), a **cyano** group (-C≡N), a **carboxylic acid** group (-COOH), a **carboxylic acid ester** group (-COOR<sup>181</sup>), a **carboxylic acid anhydride** group (-CO-O-CO- $R^{182}$ ), a **hydroxamic acid** group (-CO-NH(OH)), a **N-substituted hydroxamic acid** group (-CO-NR<sup>183</sup>(OH)), a **O-substituted hydroxamic acid** group (-CO-NH(OR<sup>184</sup>)), a **carboxamide** group (-CO-NH<sub>2</sub>), a **N-substituted or N,N-disubstituted carboxylic acid amide** group, (-CO-NHR<sup>185</sup>; -CO-NR<sup>186</sup>R<sup>187</sup>), an **amido** group (-HN-CO- $R^{188}$ ), a **sulfonic acid** group (-SO<sub>3</sub>H), a **sulfonamide** group (-SO<sub>2</sub>-NH<sub>2</sub>), a **N-substituted or N,N-disubstituted sulfonamide** group (-SO<sub>2</sub>-NHR<sup>189</sup>; -SO<sub>2</sub>-NR<sup>190</sup>R<sup>191</sup>), an **amidosulfone** group (-NH-SO<sub>2</sub>- $R^{192}$ ), a **sulfone** group (-SO<sub>2</sub>- $R^{193}$ ), a **phosphoric acid** group (-OP(=O)(OH)<sub>2</sub>), a **phosphoric acid ester** group (-OP(=O)(OR<sup>194</sup>)(OR<sup>195</sup>)), a **phosphonic acid** group (-P(=O)(OH)<sub>2</sub>), an **phosphonic acid ester** group (-P(=O)(OR<sup>196</sup>)(OR<sup>197</sup>)), a **halogen atom**, a **trifluormethyl** group (-CF<sub>3</sub>), a **thiol** group (-SH); a **thioether** group (-S- $R^{198}$ ), a **hydroxy** group (-OH); an **alkoxy** group (-O- $R^{199}$ ), a **tetrazole** group, an **amino** group (-NH<sub>2</sub>), or a **N-substituted or N,N-disubstituted amino** group (-NHR<sup>200</sup>; -NR<sup>201</sup>R<sup>202</sup>); and
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; and,

- wherein optionally, the pairs  $R^{186}/R^{187}$ ,  $R^{190}/R^{191}$ ,  $R^{194}/R^{195}$ ,  $R^{196}/R^{197}$  and  $R^{201}/R^{202}$  independently of each other, may form a part of a **ring**; and
- wherein the substituents  $R^{180}$ ,  $R^{181}$ ,  $R^{182}$ ,  $R^{183}$ ,  $R^{184}$ ,  $R^{185}$ ,  $R^{186}$ ,  $R^{187}$ ,  $R^{188}$ ,  $R^{189}$ ,  $R^{190}$ ,  $R^{191}$ ,  $R^{192}$ ,  $R^{193}$ ,  $R^{194}$ ,  $R^{195}$ ,  $R^{196}$ ,  $R^{197}$ ,  $R^{198}$ ,  $R^{199}$ ,  $R^{200}$ ,  $R^{201}$ , and  $R^{202}$ , independently of each other are a **hydrogen** atom (-H), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

or wherein the group **PM**

has the formula (IV)



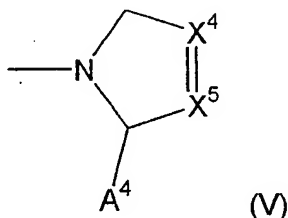
- wherein  $R^{211}$  and  $R^{212}$ , independently of each other, are
- a **hydrogen** atom (-H); or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , and  $C_5$  branched or straight chain **alkyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkenyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkinyl**,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ , and  $C_7$  **cycloalkyl**, **aryl**, **heteroaryl** group or, an **amino** group ( $-NH_2$ ), or a N-substituted or N,N-disubstituted **amino** group ( $-NHR^{240}$ ,  $-NR^{241}R^{242}$ ); and
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; and,

- wherein optionally, the pair  $R^{211}/R^{212}$ , as well the pairs  $R^{226}/R^{227}$ ,  $R^{230}/R^{231}$ ,  $R^{234}/R^{235}$ ,  $R^{236}/R^{237}$  and  $R^{241}/R^{242}$ , independently of each other, may form a part of a ring; and
- wherein the substituents  $R^{220}$ ,  $R^{221}$ ,  $R^{222}$ ,  $R^{223}$ ,  $R^{224}$ ,  $R^{225}$ ,  $R^{226}$ ,  $R^{227}$ ,  $R^{228}$ ,  $R^{229}$ ,  $R^{230}$ ,  $R^{231}$ ,  $R^{232}$ ,  $R^{233}$ ,  $R^{234}$ ,  $R^{235}$ ,  $R^{236}$ ,  $R^{237}$ ,  $R^{238}$ ,  $R^{239}$ ,  $R^{240}$ ,  $R^{241}$ , and  $R^{242}$ , independently of each other, are a **hydrogen atom** (-H), or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , and  $C_5$  branched or straight chain **alkyl**, **aryl**, **heteroaryl**, **amino**, **halo**, **carbonyl**,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkoxy**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  branched or straight chain **alkenoxy**, **phenyloxy**, **benzyloxy**,  $C_3$ ,  $C_4$ ,  $C_5$  **cycloalkyl**, **cyano**, **amido**, **thiol** **trifluoromethyl**, or **hydroxy** group; and
- wherein  $A^3$  is
- a **hydrogen atom** (-H); or a **carbaldehyde** (-CHO), a **ketone** group (-CO- $R^{260}$ ), a **boronic acid** group (-B(OH)<sub>2</sub>), a **cyano** group (-C≡N), a **carboxylic acid** group (-COOH), a **carboxylic acid ester** group (-COOR<sup>261</sup>), a **carboxylic acid anhydride** group (-CO-O-CO-R<sup>262</sup>), a **hydroxamic acid** group (-CO-NH(OH)), a **N-substituted hydroxamic acid** group (-CO-NR<sup>263</sup>(OH)), a **O-substituted hydroxamic acid** group (-CO-NH(OR<sup>264</sup>)), a **carboxamide** group (-CO-NH<sub>2</sub>), a **N-substituted or N,N-disubstituted carboxylic acid amide** group, (-CO-NHR<sup>265</sup>; -CO-NR<sup>266</sup>R<sup>267</sup>), an **amido** group (-HN-CO-R<sup>268</sup>), a **sulfonic acid** group (-SO<sub>3</sub>H), a **sulfonamide** group (-SO<sub>2</sub>-NH<sub>2</sub>), a **N-substituted or N,N-disubstituted sulfonamide** group (-SO<sub>2</sub>-NHR<sup>269</sup>; -SO<sub>2</sub>-NR<sup>270</sup>R<sup>271</sup>), an **amidosulfone** group (-NH-SO<sub>2</sub>-R<sup>272</sup>), a **sulfone** group (-SO<sub>2</sub>-R<sup>273</sup>), a **phosphoric acid** group (-OP(=O)(OH)<sub>2</sub>), a **phosphoric acid ester** group (-OP(=O)(OR<sup>274</sup>)(OR<sup>275</sup>)), a **phosphonic acid** group (-P(=O)(OH)<sub>2</sub>), an **phosphonic acid ester** group (-P(=O)(OR<sup>276</sup>)(OR<sup>277</sup>)), a **halogen atom**, a **trifluormethyl** group (-CF<sub>3</sub>), a **thiol** group (-SH); a **thioether** group (-S-R<sup>278</sup>), a **hydroxy** group (-OH); an **alkoxy** group (-O-R<sup>279</sup>), a **tetrazole** group, an **amino** group (-NH<sub>2</sub>), or a **N-substituted or N,N-disubstituted amino** group (-NHR<sup>280</sup>; -NR<sup>281</sup>R<sup>282</sup>); and

- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; and,
- wherein optionally, the pairs  $R^{266}/R^{267}$ ,  $R^{270}/R^{271}$ ,  $R^{274}/R^{275}$ ,  $R^{276}/R^{277}$  and  $R^{281}/R^{282}$ , independently of each other, may form a part of a **ring**; and
- wherein the substituents  $R^{260}$ ,  $R^{261}$ ,  $R^{262}$ ,  $R^{263}$ ,  $R^{264}$ ,  $R^{265}$ ,  $R^{266}$ ,  $R^{267}$ ,  $R^{268}$ ,  $R^{269}$ ,  $R^{270}$ ,  $R^{271}$ ,  $R^{272}$ ,  $R^{273}$ ,  $R^{274}$ ,  $R^{275}$ ,  $R^{276}$ ,  $R^{277}$ ,  $R^{278}$ ,  $R^{279}$ ,  $R^{280}$ ,  $R^{281}$ , and  $R^{282}$ , independently of each other are a **hydrogen** atom (-H), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

or wherein the group **PM**

has the formula (V)



- wherein  $X^4$  is  $CR^{291}$  or N; and
- wherein  $X^5$  is  $CR^{292}$  or N; and
- wherein  $R^{291}$  and  $R^{292}$ , independently of each other, are
- a **hydrogen** atom (-H); or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , and  $C_5$  branched or straight chain **alkyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkenyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkinyl**,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ , and  $C_7$  **cycloalkyl**, **aryl**, **heteroaryl** group or an **amino** group ( $-NH_2$ ), or a N-substituted or N,N-disubstituted **amino** group ( $-NHR^{320}$ ,  $-NR^{321}R^{322}$ ); and

- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; and,
- wherein optionally, the **the pair**  $R^{291}/R^{292}$ , if present, as well the pairs  $R^{306}/R^{307}$ ,  $R^{310}/R^{311}$ ,  $R^{314}/R^{315}$ ,  $R^{316}/R^{317}$  and  $R^{321}/R^{322}$ , independently of each other, may form a part of a **ring**; and
- wherein the substituents  $R^{300}$ ,  $R^{301}$ ,  $R^{302}$ ,  $R^{303}$ ,  $R^{304}$ ,  $R^{305}$ ,  $R^{306}$ ,  $R^{307}$ ,  $R^{308}$ ,  $R^{309}$ ,  $R^{310}$ ,  $R^{311}$ ,  $R^{312}$ ,  $R^{313}$ ,  $R^{314}$ ,  $R^{315}$ ,  $R^{316}$ ,  $R^{317}$ ,  $R^{318}$ ,  $R^{319}$ ,  $R^{320}$ ,  $R^{321}$ , and  $R^{322}$ , independently of each other are a **hydrogen atom (-H)**, or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , and  $C_5$  branched or straight chain **alkyl**, **aryl**, **heteroaryl**, **amino**, **halo**, **carbonyl**,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkoxy**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  branched or straight chain **alkenoxy**, **phenyloxy**, **benzyloxy**,  $C_3$ ,  $C_4$ ,  $C_5$  **cycloalkyl**, **cyano**, **amido**, **thiol trifluoromethyl**, or **hydroxy group**; and
- wherein  $A^4$  is
- a **hydrogen atom (-H)**; or a **carbaldehyde (-CHO)**, a **ketone group (-CO- $R^{340}$ )**, a **boronic acid group (-B(OH)<sub>2</sub>)**, a **cyano group (-C≡N)**, a **carboxylic acid group (-COOH)**, a **carboxylic acid ester group (-COOR<sup>341</sup>)**, a **carboxylic acid anhydride group (-CO-O-CO-R<sup>342</sup>)**, a **hydroxamic acid group (-CO-NH(OH))**, a **N-substituted hydroxamic acid group (-CO-NR<sup>343</sup>(OH))**, a **O-substituted hydroxamic acid group (-CO-NH(OR<sup>344</sup>))**, a **carboxamide group (-CO-NH<sub>2</sub>)**, a **N-substituted or N,N-disubstituted carboxylic acid amide group, (-CO-NHR<sup>345</sup>; -CO-NR<sup>346</sup>R<sup>347</sup>)**, an **amido group (-HN-CO-R<sup>348</sup>)**, a **sulfonic acid group (-SO<sub>3</sub>H)**, a **sulfonamide group (-SO<sub>2</sub>-NH<sub>2</sub>)**, a **N-substituted or N,N-disubstituted sulfonamide group (-SO<sub>2</sub>-NHR<sup>349</sup>; -SO<sub>2</sub>-NR<sup>350</sup>R<sup>351</sup>)**, an **amidosulfone group (-NH-SO<sub>2</sub>-R<sup>352</sup>)**, a **sulfone group (-SO<sub>2</sub>-R<sup>353</sup>)**, a **phosphoric acid group (-OP(=O)(OH)<sub>2</sub>)**, a **phosphoric acid ester group (-OP(=O)(OR<sup>354</sup>)(OR<sup>355</sup>))**, a **phosphonic acid group (-P(=O)(OH)<sub>2</sub>)**, an **phosphonic acid ester group (-P(=O)(OR<sup>356</sup>)(OR<sup>357</sup>))**, a **halogen atom**, a **trifluormethyl group (-CF<sub>3</sub>)**, a **thiol group (-SH)**; a **thioether group (-S-R<sup>358</sup>)**, a **hydroxy group (-OH)**; an **alkoxy**

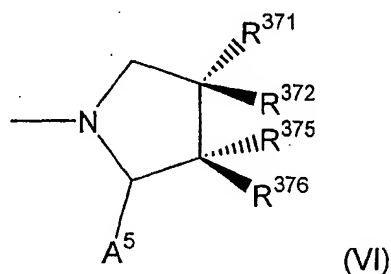


group ( $-O-R^{359}$ ), a **tetrazole** group, an **amino** group ( $-NH_2$ ), or a N-substituted or N,N-disubstituted **amino** group ( $-NHR^{360}$ ;  $-NR^{361}R^{362}$ ); and

- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; and,
- wherein optionally, the pairs  $R^{346}/R^{347}$ ,  $R^{350}/R^{351}$ ,  $R^{354}/R^{355}$ ,  $R^{356}/R^{357}$  and  $R^{361}/R^{362}$ , independently of each other, may form a part of a **ring**; and
- wherein the substituents  $R^{340}$ ,  $R^{341}$ ,  $R^{342}$ ,  $R^{343}$ ,  $R^{344}$ ,  $R^{345}$ ,  $R^{346}$ ,  $R^{347}$ ,  $R^{348}$ ,  $R^{349}$ ,  $R^{350}$ ,  $R^{351}$ ,  $R^{352}$ ,  $R^{353}$ ,  $R^{354}$ ,  $R^{355}$ ,  $R^{356}$ ,  $R^{357}$ ,  $R^{358}$ ,  $R^{359}$ ,  $R^{360}$ ,  $R^{361}$ , and  $R^{362}$ , independently of each other are a **hydrogen** atom ( $-H$ ), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

or wherein the group **PM**

has the formula (VI)



- wherein  $R^{371}$ ,  $R^{372}$ ,  $R^{375}$  and  $R^{376}$ , independently of each other, a **hydrogen** atom ( $-H$ ); or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , and  $C_5$  branched or straight chain **alkyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkenyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkinyl**,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ , and  $C_7$  **cycloalkyl**, and **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group or,

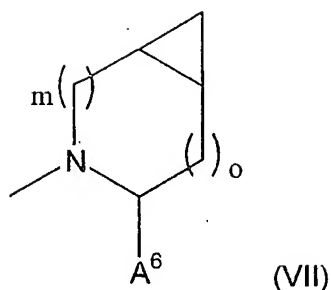
- a **carbaldehyde** (-CHO), a **ketone** group (-CO-R<sup>380</sup>), a **boronic acid** group (-B(OH)<sub>2</sub>), a **cyano** group (-C≡N), a **carboxylic acid** group (-COOH), a **carboxylic acid ester** group (-COOR<sup>381</sup>), a **halogen atom**, a **trifluormethyl** group (-CF<sub>3</sub>), a **thiol** group (-SH); a **thioether** group (-S-R<sup>398</sup>), a **hydroxy** group (-OH); an **alkoxy** group (-O-R<sup>399</sup>), a **tetrazole** group, an **amino** group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted **amino** group (-NHR<sup>400</sup>; -NR<sup>401</sup>R<sup>402</sup>); and
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; and,
  - wherein optionally, any **two of the groups** R<sup>371</sup>, R<sup>372</sup>, R<sup>375</sup>, and R<sup>376</sup>, as well as the pairs R<sup>386</sup>/R<sup>387</sup>, R<sup>390</sup>/R<sup>391</sup>, R<sup>394</sup>/R<sup>395</sup>, R<sup>396</sup>/R<sup>397</sup> and R<sup>401</sup>/R<sup>402</sup>, independently of each other, may form a part of a **ring**; and
    - wherein the substituents R<sup>380</sup>, R<sup>381</sup>, R<sup>382</sup>, R<sup>383</sup>, R<sup>384</sup>, R<sup>385</sup>, R<sup>386</sup>, R<sup>387</sup>, R<sup>388</sup>, R<sup>389</sup>, R<sup>390</sup>, R<sup>391</sup>, R<sup>392</sup>, R<sup>393</sup>, R<sup>394</sup>, R<sup>395</sup>, R<sup>396</sup>, R<sup>397</sup>, R<sup>398</sup>, R<sup>399</sup>, R<sup>400</sup>, R<sup>401</sup>, and R<sup>402</sup>, independently of each other are a **hydrogen atom** (-H), or a C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, and C<sub>5</sub> branched or straight chain **alkyl**, **aryl**, **heteroaryl**, **amino**, **halo**, **carbonyl**, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, branched or straight chain **alkoxy**, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> branched or straight chain **alkenoxy**, **phenyloxy**, **benzyloxy**, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> **cycloalkyl**, **cyano**, **amido**, **thiol** **trifluoromethyl**, or **hydroxy** group; and
  - **alternatively**; the two groups R<sup>371</sup> and R<sup>372</sup> can be together an **oxo** (=O) or **hydroxyimino** (=N-OH) group; and
  - **alternatively**; the two groups R<sup>375</sup> and R<sup>376</sup> can be together an **oxo** (=O) or **hydroxyimino** (=N-OH) group; and
  - wherein A<sup>5</sup> is
    - a **hydrogen atom** (-H); or a **carbaldehyde** (-CHO), a **ketone** group (-CO-R<sup>420</sup>), a **boronic acid** group (-B(OH)<sub>2</sub>), a **cyano** group (-C≡N), a **carboxylic acid** group (-COOH), a **carboxylic acid ester** group (-COOR<sup>421</sup>), a **carboxylic acid**

anhydride group ( $-\text{CO}-\text{O}-\text{CO}-\text{R}^{422}$ ), a hydroxamic acid group ( $-\text{CO}-\text{NH}(\text{OH})$ ), a N-substituted hydroxamic acid group ( $-\text{CO}-\text{NR}^{423}(\text{OH})$ ), a O-substituted hydroxamic acid group ( $-\text{CO}-\text{NH}(\text{OR}^{424})$ ), a carboxamide group ( $-\text{CO}-\text{NH}_2$ ), a N-substituted or N,N-disubstituted carboxylic acid amide group, ( $-\text{CO}-\text{NHR}^{425}$ ;  $-\text{CO}-\text{NR}^{426}\text{R}^{427}$ ), an amide group ( $-\text{HN}-\text{CO}-\text{R}^{428}$ ), a sulfonic acid group ( $-\text{SO}_3\text{H}$ ), a sulfonamide group ( $-\text{SO}_2-\text{NH}_2$ ), a N-substituted or N,N-disubstituted sulfonamide group ( $-\text{SO}_2-\text{NHR}^{429}$ ;  $-\text{SO}_2-\text{NR}^{430}\text{R}^{431}$ ), an amidosulfone group ( $-\text{NH}-\text{SO}_2-\text{R}^{432}$ ), a sulfone group ( $-\text{SO}_2-\text{R}^{433}$ ), a phosphoric acid group ( $-\text{OP}(=\text{O})(\text{OH})_2$ ), a phosphoric acid ester group ( $-\text{OP}(=\text{O})(\text{OR}^{434})(\text{OR}^{435})$ ), a phosphonic acid group ( $-\text{P}(=\text{O})(\text{OH})_2$ ), an phosphonic acid ester group ( $-\text{P}(=\text{O})(\text{OR}^{436})(\text{OR}^{437})$ ), a halogen atom, a trifluormethyl group ( $-\text{CF}_3$ ), a thiol group ( $-\text{SH}$ ); a thioether group ( $-\text{S}-\text{R}^{438}$ ), a hydroxy group ( $-\text{OH}$ ); an alkoxy group ( $-\text{O}-\text{R}^{439}$ ), a tetrazole group, an amino group ( $-\text{NH}_2$ ), or a N-substituted or N,N-disubstituted amino group ( $-\text{NHR}^{440}$ ;  $-\text{NR}^{441}\text{R}^{442}$ ); and

- which, independently of each other, can be substituted with one or more substituents, which can be the same or different; and,
- wherein optionally, the pairs  $\text{R}^{426}/\text{R}^{427}$ ,  $\text{R}^{430}/\text{R}^{431}$ ,  $\text{R}^{434}/\text{R}^{435}$ ,  $\text{R}^{436}/\text{R}^{437}$  and  $\text{R}^{441}/\text{R}^{442}$ , independently of each other, may form a part of a ring; and
- wherein the substituents  $\text{R}^{420}$ ,  $\text{R}^{421}$ ,  $\text{R}^{422}$ ,  $\text{R}^{423}$ ,  $\text{R}^{424}$ ,  $\text{R}^{425}$ ,  $\text{R}^{426}$ ,  $\text{R}^{427}$ ,  $\text{R}^{428}$ ,  $\text{R}^{429}$ ,  $\text{R}^{430}$ ,  $\text{R}^{431}$ ,  $\text{R}^{432}$ ,  $\text{R}^{433}$ ,  $\text{R}^{434}$ ,  $\text{R}^{435}$ ,  $\text{R}^{436}$ ,  $\text{R}^{437}$ ,  $\text{R}^{438}$ ,  $\text{R}^{439}$ ,  $\text{R}^{440}$ ,  $\text{R}^{441}$ , and  $\text{R}^{442}$ , independently of each other are a hydrogen atom ( $-\text{H}$ ), or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group;

or wherein the group PM

has the formula (VII)

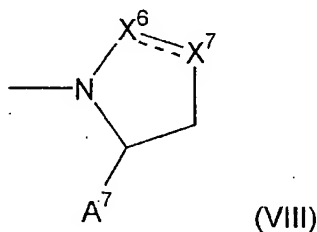


- wherein m is equal to 1 or 2, and o is equal to 1 or 2, and m or o can be equal to 0;
- wherein  $A^6$  is a **hydrogen atom** (-H); or a **carbaldehyde** (-CHO), a **ketone group** (-CO-R<sup>460</sup>), a **boronic acid group** (-B(OH)<sub>2</sub>), a **cyano group** (-C≡N), a **carboxylic acid group** (-COOH), a **carboxylic acid ester group** (-COOR<sup>461</sup>), a **carboxylic acid anhydride group** (-CO-O-CO-R<sup>462</sup>), a **hydroxamic acid group** (-CO-NH(OH)), a **N-substituted hydroxamic acid group** (-CO-NR<sup>463</sup>(OH)), a **O-substituted hydroxamic acid group** (-CO-NH(OR<sup>464</sup>)), a **carboxamide group** (-CO-NH<sub>2</sub>), a **N-substituted or N,N-disubstituted carboxylic acid amide group**, (-CO-NHR<sup>465</sup>; -CO-NR<sup>466</sup>R<sup>467</sup>), an **amido group** (-HN-CO-R<sup>468</sup>), a **sulfonic acid group** (-SO<sub>3</sub>H), a **sulfonamide group** (-SO<sub>2</sub>-NH<sub>2</sub>), a **N-substituted or N,N-disubstituted sulfonamide group** (-SO<sub>2</sub>-NHR<sup>469</sup>; -SO<sub>2</sub>-NR<sup>470</sup>R<sup>471</sup>), an **amidosulfone group** (-NH-SO<sub>2</sub>-R<sup>472</sup>), a **sulfone group** (-SO<sub>2</sub>-R<sup>473</sup>), a **phosphoric acid group** (-OP(=O)(OH)<sub>2</sub>), a **phosphoric acid ester group** (-OP(=O)(OR<sup>474</sup>)(OR<sup>475</sup>)), a **phosphonic acid group** (-P(=O)(OH)<sub>2</sub>), an **phosphonic acid ester group** (-P(=O)(OR<sup>476</sup>)(OR<sup>477</sup>)), a **halogen atom**, a **trifluormethyl group** (-CF<sub>3</sub>), a **thiol group** (-SH); a **thioether group** (-S-R<sup>478</sup>), a **hydroxy group** (-OH); an **alkoxy group** (-O-R<sup>479</sup>), a **tetrazole group**, an **amino group** (-NH<sub>2</sub>), or a **N-substituted or N,N-disubstituted amino group** (-NHR<sup>480</sup>; -NR<sup>481</sup>R<sup>482</sup>);
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; and,

- wherein optionally, the pairs  $R^{466}/R^{467}$ ,  $R^{470}/R^{471}$ ,  $R^{474}/R^{475}$ ,  $R^{476}/R^{477}$  and  $R^{481}/R^{482}$ , independently of each other, may form a part of a ring; and
- wherein the substituents  $R^{460}$ ,  $R^{461}$ ,  $R^{462}$ ,  $R^{463}$ ,  $R^{464}$ ,  $R^{465}$ ,  $R^{466}$ ,  $R^{467}$ ,  $R^{468}$ ,  $R^{469}$ ,  $R^{470}$ ,  $R^{471}$ ,  $R^{472}$ ,  $R^{473}$ ,  $R^{474}$ ,  $R^{475}$ ,  $R^{476}$ ,  $R^{477}$ ,  $R^{478}$ ,  $R^{479}$ ,  $R^{480}$ ,  $R^{481}$ , and  $R^{482}$ , independently of each other are a hydrogen atom (-H), or an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkinyl, heteroalkyl, heteroalkenyl, heteroalkinyl, heterocycloalkyl, heterocycloalkenyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, aryl-heteroalkyl, heteroaryl-heteroalkyl group;

or wherein the group PM

has the formula (VIII)



- wherein  $X^6$  is selected from  $CR^{490}R^{491}$ , O, S or  $NR^{492}$ , when the bond between  $X^6$  and  $X^7$  is a single bond; and
- wherein  $X^7$  is selected from  $CR^{493}R^{494}$ , O, S, or  $NR^{495}$ , when the bond between  $X^6$  and  $X^7$  is a single bond;
- or alternatively,
- wherein  $X^6$  is selected from  $CR^{496}$  or N, when the bond between  $X^6$  and  $X^7$  is a double bond; and
- wherein  $X^7$  is selected from  $CR^{497}$  or N, when the bond between  $X^6$  and  $X^7$  is a double bond; and
- wherein  $R^{490}$ ,  $R^{491}$ ,  $R^{492}$ ,  $R^{493}$ ,  $R^{494}$ ,  $R^{495}$ ,  $R^{496}$ , and  $R^{497}$ , independently of each other, are a hydrogen atom (-H); or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , and  $C_5$  branched or straight

chain **alkyl**, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, branched or straight chain **alkenyl**, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, branched or straight chain **alkinyl**, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, and C<sub>7</sub> **cycloalkyl**, **aryl**, **heteroaryl** group, or an **amino** group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted **amino** group (-NHR<sup>520</sup>, -NR<sup>521</sup>R<sup>522</sup>); and

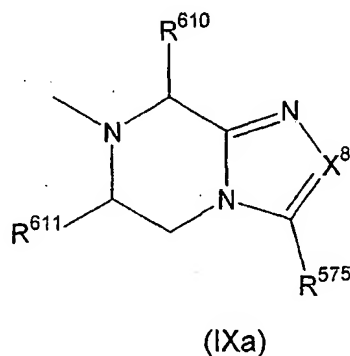
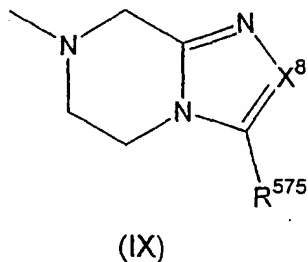
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; and,
- wherein optionally, any two the groups R<sup>490</sup>, R<sup>491</sup>, R<sup>492</sup>, R<sup>493</sup>, R<sup>494</sup>, R<sup>495</sup>, R<sup>496</sup>, and R<sup>497</sup>, if present, as well as the pairs R<sup>506</sup>/R<sup>507</sup>, R<sup>510</sup>/R<sup>511</sup>, R<sup>514</sup>/R<sup>515</sup>, R<sup>516</sup>/R<sup>517</sup> and R<sup>521</sup>/R<sup>522</sup>, independently of each other, may form a part of a ring; and
- wherein the substituents R<sup>500</sup>, R<sup>501</sup>, R<sup>502</sup>, R<sup>503</sup>, R<sup>504</sup>, R<sup>505</sup>, R<sup>506</sup>, R<sup>507</sup>, R<sup>508</sup>, R<sup>509</sup>, R<sup>510</sup>, R<sup>511</sup>, R<sup>512</sup>, R<sup>513</sup>, R<sup>514</sup>, R<sup>515</sup>, R<sup>516</sup>, R<sup>517</sup>, R<sup>518</sup>, R<sup>519</sup>, R<sup>520</sup>, R<sup>521</sup>, and R<sup>522</sup>, independently of each other are a **hydrogen** atom (-H), or a C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, and C<sub>5</sub> branched or straight chain **alkyl**, **aryl**, **heteroaryl**, **amino**, **halo**, **carbonyl**, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, branched or straight chain **alkoxy**, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> branched or straight chain **alkenoxy**, **phenyloxy**, **benzyloxy**, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> **cycloalkyl**, **cyano**, **amido**, **thiol** **trifluoromethyl**, or **hydroxy** group; and
- wherein A<sup>7</sup> is
- a **hydrogen** atom (-H); or a **carbaldehyde** (-CHO), a **ketone** group (-CO-R<sup>540</sup>), a **boronic acid** group (-B(OH)<sub>2</sub>), a **cyano** group (-C≡N), a **carboxylic acid** group (-COOH), a **carboxylic acid ester** group (-COOR<sup>541</sup>), a **carboxylic acid anhydride** group (-CO-O-CO-R<sup>542</sup>), a **hydroxamic acid** group (-CO-NH(OH)), a N-substituted **hydroxamic acid** group (-CO-NR<sup>543</sup>(OH)), a O-substituted **hydroxamic acid** group (-CO-NH(OR<sup>544</sup>)), a **carboxamide** group (-CO-NH<sub>2</sub>), a N-substituted or N,N-disubstituted **carboxylic acid amide** group, (-CO-NHR<sup>545</sup>, -CO-NR<sup>546</sup>R<sup>547</sup>), an **amido** group (-HN-CO-R<sup>548</sup>), a **sulfonic acid** group (-SO<sub>3</sub>H), a **sulfonamide** group (-SO<sub>2</sub>-NH<sub>2</sub>), a N-substituted or N,N-disubstituted **sulfonamide** group (-SO<sub>2</sub>-NHR<sup>549</sup>, -SO<sub>2</sub>-NR<sup>550</sup>R<sup>551</sup>), an **amidosulfone** group (-NH-SO<sub>2</sub>-R<sup>552</sup>), a **sulfone** group (-SO<sub>2</sub>-R<sup>553</sup>), a **phosphoric acid** group

(-OP(=O)(OH)<sub>2</sub>), a **phosphoric acid ester** group (-OP(=O)(OR<sup>554</sup>)(OR<sup>555</sup>)), a **phosphonic acid** group (-P(=O)(OH)<sub>2</sub>), an **phosphonic acid ester** group (-P(=O)(OR<sup>556</sup>)(OR<sup>557</sup>)), a **halogen atom**, a **trifluormethyl** group (-CF<sub>3</sub>), a **thiol** group (-SH); a **thioether** group (-S-R<sup>558</sup>), a **hydroxy** group (-OH); an **alkoxy** group (-O-R<sup>559</sup>), a **tetrazole** group, an **amino** group (-NH<sub>2</sub>), or a **N-substituted** or **N,N-disubstituted amino** group (-NHR<sup>560</sup>; -NR<sup>561</sup>R<sup>562</sup>); and

- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the pairs R<sup>546</sup>/R<sup>547</sup>, R<sup>550</sup>/R<sup>551</sup>, R<sup>554</sup>/R<sup>555</sup>, R<sup>556</sup>/R<sup>557</sup> and R<sup>561</sup>/R<sup>562</sup>, independently of each other, may form a part of a **ring**; and
- wherein the substituents R<sup>540</sup>, R<sup>541</sup>, R<sup>542</sup>, R<sup>543</sup>, R<sup>544</sup>, R<sup>545</sup>, R<sup>546</sup>, R<sup>547</sup>, R<sup>548</sup>, R<sup>549</sup>, R<sup>550</sup>, R<sup>551</sup>, R<sup>552</sup>, R<sup>553</sup>, R<sup>554</sup>, R<sup>555</sup>, R<sup>556</sup>, R<sup>557</sup>, R<sup>558</sup>, R<sup>559</sup>, R<sup>560</sup>, R<sup>561</sup>, and R<sup>562</sup>, independently of each other are a **hydrogen atom** (-H), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

or wherein the group **PM**

has the formula (IX) or (IXa)



- wherein  $X^8$  is N or  $CR^{570}$ ; and
- wherein  $R^{570}$ ,  $R^{575}$ ,  $R^{610}$  and  $R^{611}$  independently of each other, are
 

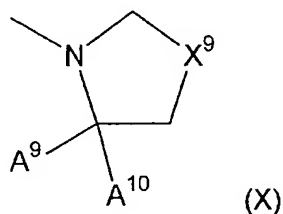
a **hydrogen** atom (-H); or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , and  $C_5$  branched or straight chain **alkyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkenyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkinyl**,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ , and  $C_7$  **cycloalkyl**, **aryl**, **heteroaryl** group, or a **carbaldehyde** (-CHO), a **ketone** group ( $-CO-R^{580}$ ), a **boronic acid** group ( $-B(OH)_2$ ), a **cyano** group ( $-C\equiv N$ ), a **carboxylic acid** group ( $-COOH$ ), a **carboxylic acid ester** group ( $-COOR^{581}$ ), a **carboxylic acid anhydride** group ( $-CO-O-CO-R^{582}$ ), a **hydroxamic acid** group ( $-CO-NH(OH)$ ), a N-substituted **hydroxamic acid** group ( $-CO-NR^{583}(OH)$ ), a O-substituted **hydroxamic acid** group ( $-CO-NH(OR^{584})$ ), a **carboxamide** group ( $-CO-NH_2$ ), a N-substituted or N,N-disubstituted **carboxylic acid amide** group, ( $-CO-NHR^{585}$ ;  $-CO-NR^{586}R^{587}$ ), an **amido** group ( $-HN-CO-R^{588}$ ), a **sulfonic acid** group ( $-SO_3H$ ), a **sulfonamide** group ( $-SO_2-NH_2$ ), a N-substituted or N,N-disubstituted **sulfonamide** group ( $-SO_2-NHR^{589}$ ;  $-SO_2-NR^{590}R^{591}$ ), an **amidosulfone** group ( $-NH-SO_2-R^{592}$ ), a **sulfone** group ( $-SO_2-R^{593}$ ), a **phosphoric acid** group ( $-OP(=O)(OH)_2$ ), a **phosphoric acid ester** group ( $-OP(=O)(OR^{594})(OR^{595})$ ), a **phosphonic acid** group ( $-P(=O)(OH)_2$ ), an **phosphonic acid ester** group ( $-P(=O)(OR^{596})(OR^{597})$ ), a **halogen atom**, a **trifluormethyl** group ( $-CF_3$ ), a **thiol** group ( $-SH$ ); a **thioether** group ( $-S-R^{598}$ ), a **hydroxy** group ( $-OH$ ); an **alkoxy** group ( $-O-R^{599}$ ), a **tetrazole** group, an **amino** group ( $-NH_2$ ), or a N-substituted or N,N-disubstituted **amino** group ( $-NHR^{600}$ ;  $-NR^{601}R^{602}$ );
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; and,
- wherein optionally, the pairs  $R^{570}/R^{575}$ , if present, as well as the pairs  $R^{586}/R^{587}$ ,  $R^{590}/R^{591}$ ,  $R^{594}/R^{595}$ ,  $R^{596}/R^{597}$  and  $R^{601}/R^{602}$ , independently of each other, may form a part of a ring; and



- wherein the substituents  $R^{580}$ ,  $R^{581}$ ,  $R^{582}$ ,  $R^{583}$ ,  $R^{584}$ ,  $R^{585}$ ,  $R^{586}$ ,  $R^{587}$ ,  $R^{588}$ ,  $R^{589}$ ,  $R^{590}$ ,  $R^{591}$ ,  $R^{592}$ ,  $R^{593}$ ,  $R^{594}$ ,  $R^{595}$ ,  $R^{596}$ ,  $R^{597}$ ,  $R^{598}$ ,  $R^{599}$ ,  $R^{600}$ ,  $R^{601}$ , and  $R^{602}$ , independently of each other are a **hydrogen** atom (-H), or a C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, and C<sub>5</sub> branched or straight chain **alkyl**, **aryl**, **heteroaryl**, **amino**, **halo**, **carbonyl**, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, branched or straight chain **alkoxy**, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> branched or straight chain **alkenoxy**, **phenyloxy**, **benzyloxy**, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> **cycloalkyl**, **cyano**, **amido**, **thiol** **trifluoromethyl**, or **hydroxy** group; and

or wherein the group PM

has the formula (X)



- wherein the groups  $X^9$  is  $CR^{900}R^{901}$ , S, SO, SO<sub>2</sub> or  $NR^{902}$ 
  - wherein  $R^{900}$ ,  $R^{901}$  and  $R^{902}$ , are, independently of each other, selected from hydrogen, fluorine, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens, or  $-C(=O)NR^{910}R^{911}$ .
- wherein  $A^9$  and  $A^{10}$  are, independently of each other, selected from hydrogen, cyano,  $-C(=O)NR^{912}R^{913}$ , or C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein

- $R^{910}$  and  $R^{912}$ , are, independently of each other, selected from hydrogen, or C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens; and

- $R^{911}$  and  $R^{913}$ , are, independently of each other, selected from the group consisting of

(1) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5, substituents independently selected from halogen and  $R^{920}$ ;

(2)  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6 or 7 substituents independently selected from (a) 0, 1, 2, 3, 4, or 5 halogens, and (b) 0, 1, 2 substituents selected from the group consisting of

(a) hydroxy,

(b)  $-COOH$ ,

(c)  $-COO(C_1, C_2, C_3, C_4, C_5 \text{ or } C_6 \text{ alkyl})$ , i.e. ester,

(d) phenyl,

(e) naphthyl,

(f)  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  cycloalkyl,

(g) a 5 - or 6 membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur;

(h) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (a) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (b) a benzene ring fused to a 5- or 6-membered heterocycle having 1, 2, or 3 hetero atoms;

- wherein said  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  cycloalkyl, phenyl, naphthyl, are optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from halogen and  $R^{920}$ , and said 5 or 6 membered heterocycle and said 8, 9 or 10 - membered bicyclic ring system are each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, and  $R^{920}$ ; and

(3)  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  cycloalkyl, which is optionally substituted with 1, 2, or 3 groups independently selected from halogen, hydroxy,  $-COOH$ ,  $-COO(C_1, C_2, C_3, C_4, C_5 \text{ or } C_6 \text{ alkyl})$ , i.e. ester,  $C_1, C_2, C_3, C_4, C_5$  or  $C_6$  alkyl, and  $-OC_1, -OC_2, -OC_3, -OC_4, -OC_5$  or  $-OC_6$  alkyl, said  $-COO(C_1, C_2, C_3, C_4, C_5 \text{ or } C_6 \text{ alkyl})$ , i.e. ester,  $C_1, C_2, C_3, C_4, C_5$  or  $C_6$  alkyl, and  $-OC_1, -OC_2, -OC_3, -OC_4,$

-OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein R<sup>920</sup> is selected from the group consisting of:

- (1) hydroxy;
- (2) cyano;
- (3) C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl optionally substituted with 1, 2, or 3 groups independently selected from halogen, hydroxy, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, wherein said -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl are linear or branched and are optionally substituted with 1, 2, 3, 4, 5 or 6 substituents selected from 1, 2, 3, 4, or 5 halogens, and 0 or 1 substituents selected from -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, -COOH, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl substituents being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;
- (4) C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub>, C<sub>9</sub> or C<sub>10</sub> alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6, or 7 substituents independently selected from 0, 1, 2, 3, 4, or 5 halogen atoms and 0, 1, or 2 groups selected from
  - (a) hydroxy;
  - (b) -COOH;
  - (c) -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, which may linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens;
  - (d) a 5 - or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.;
  - (e) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (i) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (ii) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen ,

oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(f) -CONR<sup>925</sup>R<sup>925</sup>;

(g) -SO<sub>2</sub>NR<sup>925</sup>R<sup>925</sup>;

(h) -NR<sup>925</sup>-C(=O)R<sup>925</sup>;

(i) -NR<sup>925</sup>-C(=O)NR<sup>925</sup>R<sup>925</sup>;

(j) -NR<sup>925</sup>COOR<sup>930</sup>;

(k) -O-CO-R<sup>930</sup>;

(l) -O-CO-NR<sup>925</sup>R<sup>925</sup>;

(m) -NR<sup>925</sup>SO<sub>2</sub>R<sup>930</sup>;

(n) -NR<sup>925</sup>R<sup>925</sup>;

(o) phenyl which is optionally substituted with 1, 2, 3, 4, or 5 group independently selected from halogen, hydroxy, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, 5, or 6 substituents independently selected from 0 or 1 C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl and 0, 1, 2, 3, 4, or 5 halogens, and

(p) C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl, which is optionally substituted with 1, 2, 3, 4, 5, or 6 halogens;

(5) OC<sub>1</sub>, OC<sub>2</sub>, OC<sub>3</sub>, OC<sub>4</sub>, OC<sub>5</sub>, OC<sub>6</sub>, OC<sub>7</sub>, OC<sub>8</sub>, OC<sub>9</sub> or OC<sub>10</sub> alkyl, which is linear or branched and is optionally substituted with 0, 1, 2, 3, 4, or 5 halogen atoms and 0, 1, or 2 substituents selected from

(a) hydroxy;

(b) -COOH;

(c) -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, which may be linear or branched and is optionally substituted with 1, 2, 3, 4 or 5 halogens;

(d) a 5 - or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>,

C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.;

(e) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (i) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (ii) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(f) -CONR<sup>925</sup>R<sup>925</sup>;

(g) -SO<sub>2</sub>NR<sup>925</sup>R<sup>925</sup>;

(h) -NR<sup>925</sup>-C(=O)R<sup>925</sup>;

(i) -NR<sup>925</sup>-C(=O)NR<sup>925</sup>R<sup>925</sup>;

(j) -NR<sup>925</sup>COOR<sup>930</sup>;

(k) -O-CO-R<sup>930</sup>;

(l) -O-CO-NR<sup>925</sup>R<sup>925</sup>;

(m) -NR<sup>925</sup>SO<sub>2</sub>R<sup>930</sup>;

(n) -NR<sup>925</sup>R<sup>925</sup>;

(o) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5 groups independently selected from halogen, hydroxy, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, 5, or 6 substituents independently selected from 0 or 1 C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl and 0, 1, 2, 3, 4, or 5 halogens, and

(p) C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl, which is optionally substituted with 1, 2, 3, 4, 5, or 6 halogens;

(6) -COOH;

(7)  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester, which may be linear or branched and is optionally substituted with 1, 2, 3, 4, 5 halogens;

(8) a 5 - or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3; or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, said heterocycle being optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen,  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5 \text{ or } -\text{OC}_6$  alkyl, said  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5 \text{ or } -\text{OC}_6$  alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.

(9) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (a) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (b) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen,  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5 \text{ or } -\text{OC}_6$  alkyl, said  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5 \text{ or } -\text{OC}_6$  alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(10)  $-\text{CONR}^{925}\text{R}^{925}$ ;

(11)  $-\text{SO}_2\text{NR}^{925}\text{R}^{925}$ ;

(12)  $-\text{NR}^{925}-\text{C}(=\text{O})\text{R}^{925}$

(13)  $-\text{NR}^{925}-\text{C}(=\text{O})\text{NR}^{925}\text{R}^{925}$ ;

(14)  $-\text{NR}^{925}\text{COOR}^{930}$

(15)  $-\text{O}-\text{CO}-\text{R}^{930}$

(16)  $-\text{O}-\text{CO}-\text{NR}^{925}\text{R}^{925}$ ;

(17)  $-\text{NR}^{925}\text{SO}_2\text{R}^{930}$ ;

(18)  $-\text{NR}^{925}\text{R}^{925}$ ;

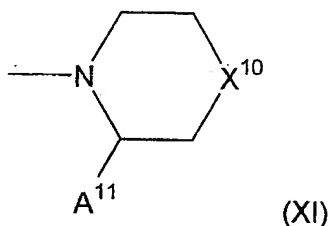
(19) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5 group independently selected from halogen, hydroxy,  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6$  alkyl,  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5 \text{ or } -\text{OC}_6$  alkyl,  $-\text{COOH}, -\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester, said  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6$  alkyl,  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5 \text{ or } -\text{OC}_6$  alkyl,  $-\text{COOH}, -\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein  $R^{930}$  is selected from the group consisting of phenyl,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  cycloalkyl, and  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  cycloalkyl, wherein  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6, substituents independently selected from 0, 1, 2, 3, 4, or 5 halogens, 0 or 1 phenyl, wherein said optional phenyl substituent and said  $R^{930}$ , when  $R^{930}$  is phenyl or  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  cycloalkyl, are optionally substituted with 1, 2, 3, 4, or 5 substituents, independently selected from halogen, OH,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , or  $C_5$  alkyl,  $-OC_1$ ,  $-OC_2$ ,  $-OC_3$ ,  $-OC_4$ , or  $-OC_5$  alkyl, said  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , or  $C_5$  alkyl,  $-OC_1$ ,  $-OC_2$ ,  $-OC_3$ ,  $-OC_4$ , or  $-OC_5$  alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.

wherein  $R^{925}$  is selected from  $R^{930}$  and hydrogen.

wherein the group PM

has the formula (XI)



- wherein the groups  $X^{10}$  is  $CR^{1000}R^{1001}$ , S, SO,  $SO_2$  or  $NR^{1002}$ 
  - wherein  $R^{1000}$ ,  $R^{1001}$  and  $R^{1002}$ , are, independently of each other, selected from hydrogen, fluorine,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens, or  $-C(=O)NR^{1010}R^{1011}$ .

and  $A^{11}$  is selected from

hydrogen, cyano,  $-C(=O)NR^{1012}R^{1013}$ , or  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein

- $R^{1010}$  and  $R^{1012}$ , are, independently of each other, selected from hydrogen, or  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens; and
- $R^{1011}$  and  $R^{1013}$ , are, independently of each other, selected from the group consisting of

(1) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5, substituents independently selected from halogen and  $R^{1020}$ ;

(2)  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6 or 7 substituents independently selected from (a) 0, 1, 2, 3, 4, or 5 halogens, and (b) 0, 1, 2 substituents selected from the group consisting of

- (a) hydroxy,
- (b) -COOH,
- (c) -COO( $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl), i.e. ester,
- (d) phenyl,
- (e) naphthyl,
- (f)  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  cycloalkyl,
- (g) a 5 - or 6 membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur;
- (h) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (a) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (b) a benzene ring fused to a 5- or 6-membered heterocycle having 1, 2, or 3 hetero atoms;

- wherein said  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  cycloalkyl, phenyl, naphthyl, are optionally substituted with 1, 2, 3, 4, or 5 substituents independently



selected from halogen and  $R^{1020}$ , and said 5 or 6 membered heterocycle and said 8, 9 or 10 - membered bicyclic ring system are each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from from oxo, hydroxy, halogen, and  $R^{1020}$ ; and

(3)  $C_3$ ,  $C_4$   $C_5$  or  $C_6$  cycloalkyl, which is optionally substituted with 1, 2, or 3 groups independently selected from halogen, hydroxy,  $-COOH$ ,  $-COO(C_1, C_2, C_3, C_4, C_5$  or  $C_6$  alkyl), i.e. ester,  $C_1, C_2, C_3, C_4, C_5$  or  $C_6$  alkyl, and  $-OC_1, -OC_2, -OC_3, -OC_4, -OC_5$  or  $-OC_6$  alkyl, said  $-COO(C_1, C_2, C_3, C_4, C_5$  or  $C_6$  alkyl), i.e. ester,  $C_1, C_2, C_3, C_4, C_5$  or  $C_6$  alkyl, and  $-OC_1, -OC_2, -OC_3, -OC_4, -OC_5$  or  $-OC_6$  alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein  $R^{1020}$  is selected from the group consisting of:

(1) hydroxy;

(2) cyano;

(3)  $C_3, C_4, C_5$  or  $C_6$  cycloalkyl optionally substituted with 1, 2, or 3 groups independently selected from halogen, hydroxy,  $-COOH$ ,  $-COO(C_1, C_2, C_3, C_4, C_5$  or  $C_6$  alkyl), i.e. ester,  $C_1, C_2, C_3, C_4, C_5$  or  $C_6$  alkyl, and  $-OC_1, -OC_2, -OC_3, -OC_4, -OC_5$  or  $-OC_6$  alkyl, wherein said  $-COO(C_1, C_2, C_3, C_4, C_5$  or  $C_6$  alkyl) i.e. ester,  $C_1, C_2, C_3, C_4, C_5$  or  $C_6$  alkyl, and  $-OC_1, -OC_2, -OC_3, -OC_4, -OC_5$  or  $-OC_6$  alkyl are linear or branched and are optionally substituted with 1, 2, 3, 4, 5 or 6 substituents selected from 1, 2, 3, 4, or 5 halogens, and 0 or 1 substituents selected from  $-COO(C_1, C_2, C_3, C_4, C_5$  or  $C_6$  alkyl) i.e. ester,  $-COOH$ , and  $-OC_1, -OC_2, -OC_3, -OC_4, -OC_5$  or  $-OC_6$  alkyl substituents being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(4)  $C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9$  or  $C_{10}$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6, or 7 substituents independently selected from 0, 1, 2, 3, 4, or 5 halogen atoms and 0, 1, or 2 groups selected from

(a) hydroxy;

(b)  $-COOH$ ;

(c)  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester, which may linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens;

(d) a 5 - or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen,  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5 \text{ or } -\text{OC}_6$  alkyl, said  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5 \text{ or } -\text{OC}_6$  alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.;

(e) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (i) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (ii) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen,  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5 \text{ or } -\text{OC}_6$  alkyl, said  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5 \text{ or } -\text{OC}_6$  alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(f)  $-\text{CONR}^{1025}\text{R}^{1025}$ ;

(g)  $-\text{SO}_2\text{NR}^{1025}\text{R}^{1025}$ ;

(h)  $-\text{NR}^{1025}-\text{C}(=\text{O})\text{R}^{1025}$

(i)  $-\text{NR}^{1025}-\text{C}(=\text{O})\text{NR}^{1025}\text{R}^{1025}$ ;

(j)  $-\text{NR}^{1025}\text{COOR}^{1030}$

(k)  $-\text{O}-\text{CO}-\text{R}^{1030}$

(l)  $-\text{O}-\text{CO}-\text{NR}^{1025}\text{R}^{1025}$ ;

(m)  $-\text{NR}^{1025}\text{SO}_2\text{R}^{1030}$ ;

(n)  $-\text{NR}^{1025}\text{R}^{1025}$ ;

(o) phenyl which is optionally substituted with 1, 2, 3, 4, or 5 group independently selected from halogen, hydroxy, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, 5, or 6 substituents independently selected from 0 or 1 C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl and 0, 1, 2, 3, 4, or 5 halogens, and

(p) C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl, which is optionally substituted with 1, 2, 3, 4, 5, or 6 halogens;

(5) OC<sub>1</sub>, OC<sub>2</sub>, OC<sub>3</sub>, OC<sub>4</sub>, OC<sub>5</sub>, OC<sub>6</sub>, OC<sub>7</sub>, OC<sub>8</sub>, OC<sub>9</sub> or OC<sub>10</sub> alkyl, which is linear or branched and is optionally substituted with 0, 1, 2, 3, 4, or 5 halogen atoms and 0, 1, or 2 substituents selected from

(a) hydroxy;

(b) -COOH;

(c) -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, which may be linear or branched and is optionally substituted with 1, 2, 3, 4 or 5 halogens;

(d) a 5 - or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.;

(e) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (i) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (ii) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents

independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(f) -CONR<sup>1025</sup>R<sup>1025</sup>;

(g) -SO<sub>2</sub>NR<sup>1025</sup>R<sup>1025</sup>;

(h) -NR<sup>1025</sup>-C(=O)R<sup>1025</sup>

(i) -NR<sup>1025</sup>-C(=O)NR<sup>1025</sup>R<sup>1025</sup>;

(j) -NR<sup>1025</sup>COOR<sup>1030</sup>

(k) -O-CO-R<sup>1030</sup>

(l) -O-CO-NR<sup>1025</sup>R<sup>1025</sup>;

(m) -NR<sup>1025</sup>SO<sub>2</sub>R<sup>1030</sup>;

(n) - NR<sup>1025</sup>R<sup>1025</sup>;

(o) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5 groups independently selected from halogen, hydroxy, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, 5, or 6 substituents independently selected from 0 or 1 C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl and 0, 1, 2, 3, 4, or 5 halogens, and

(p) C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, which is optionally substituted with 1, 2, 3, 4, 5, or 6 halogens;

(6) -COOH;

(7) -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, which may be linear or branched and is optionally substituted with 1, 2, 3, 4, 5 halogens;

(8) a 5 - or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, said heterocycle being optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>,

C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.

(9) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (a) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (b) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(10) -CONR<sup>1025</sup>R<sup>1025</sup>;

(11) -SO<sub>2</sub>NR<sup>1025</sup>R<sup>1025</sup>;

(12) -NR<sup>1025</sup>-C(=O)R<sup>1025</sup>

(13) -NR<sup>1025</sup>-C(=O)NR<sup>1025</sup>R<sup>1025</sup>;

(14) -NR<sup>925</sup>COOR<sup>1030</sup>

(15) -O-CO-R<sup>1030</sup>

(16) -O-CO-NR<sup>1025</sup>R<sup>1025</sup>;

(17) -NR<sup>1025</sup>SO<sub>2</sub>R<sup>1030</sup>;

(18) -NR<sup>1025</sup>R<sup>1025</sup>;

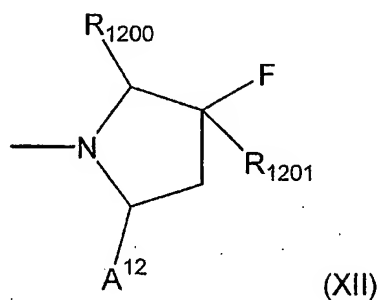
(19) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5 group independently selected from halogen, hydroxy, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein  $R^{1030}$  is selected from the group consisting of phenyl,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  cycloalkyl, and  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  cycloalkyl, wherein  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6, substituents independently selected from 0, 1, 2, 3, 4, or 5 halogens, 0 or 1 phenyl, wherein said optional phenyl substituent and said  $R^{930}$ , when  $R^{930}$  is phenyl or  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  cycloalkyl, are optionally substituted with 1, 2, 3, 4, or 5 substituents, independently selected from halogen, OH,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , or  $C_5$  alkyl,  $-OC_1$ ,  $-OC_2$ ,  $-OC_3$ ,  $-OC_4$ , or  $-OC_5$  alkyl, said  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , or  $C_5$  alkyl,  $-OC_1$ ,  $-OC_2$ ,  $-OC_3$ ,  $-OC_4$ , or  $-OC_5$  alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.

wherein  $R^{1025}$  is selected from  $R^{1030}$  and hydrogen.

or wherein the group PM

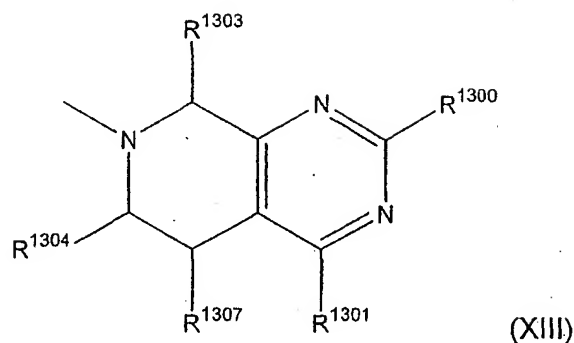
has the formula (XII)



- wherein the groups  $R^{1201}$  is hydrogen or fluoro.
- wherein  $R^{1200}$  and  $A^{12}$  is selected from hydrogen and cyano, and the other is hydrogen.

or wherein the group PM

has the formula XIII:



wherein:

-  $R^{1300}$  is selected from the group consisting of:

- (10) hydrogen,
- (11) CN,
- (12)  $C_{1-10}$ alkyl, which is linear or branched and which is unsubstituted or substituted with:
  - a) halogen, or
  - b) phenyl, which is unsubstituted or substituted with 1 - 5 substituents independently selected from halogen, CN, OH,  $R^{1302}$ ,  $OR^{1302}$ ,  $NHSO_2R^{1302}$ ,  $N(C_{1-6}alkyl)SO_2R^{1302}$ ,  $SO_2R^{1302}$ ,  $SO_2NR^{1305}R^{1306}$ ,  $NR^{1305}R^{1306}$ ,  $CONR^{1305}R^{1306}$ ,  $CO_2H$ , and  $CO_2C_{1-6}alkyl$ , wherein the  $C_{1-6}alkyl$  is linear or branched,
- (13) phenyl which is unsubstituted or substituted with 1 - 5 substituents independently selected from halogen, CN, OH,  $R^{1302}$ ,  $OR^{1302}$ ,  $NHSO_2R^{1302}$ ,

$N(C_{1-6}\text{alkyl})SO_2R^{1302}$ ,  $SO_2R^{1302}$ ,  $SO_2NR^{1305}R^{1306}$ ,  $NR^{1305}R^{1306}$ ,  $CONR^{1305}R^{1306}$ ,  $CO_2H$ , and  $CO_2C_{1-6}\text{alkyl}$ , wherein the  $C_{1-6}\text{alkyl}$  is linear or branched,

(14) a 5- or 6-membered heterocyclic which may be saturated or unsaturated comprising 1 – 4 heteroatoms independently selected from N, S and O, the heterocycle being unsubstituted or substituted with 1 – 3 substituents independently selected from oxo, halogen,  $NO_2$ , CN, OH,  $R^{1302}$ ,  $OR^{1302}$ ,  $NHSO_2R^{1302}$ ,  $N(C_{1-6}\text{alkyl})SO_2R^{1302}$ ,  $SO_2R^{1302}$ ,  $SO_2NR^{1305}R^{1306}$ ,  $NR^{1305}R^{1306}$ ,  $CONR^{1305}R^{1306}$ ,  $CO_2H$ , and  $CO_2C_{1-6}\text{alkyl}$ , wherein the  $C_{1-6}\text{alkyl}$  is linear or branched,

(15)  $C_{3-6}\text{cycloalkyl}$ , which is optionally substituted with 1 – 5 substituents independently selected from halogen, OH,  $C_{1-6}\text{alkyl}$ , and  $OC_{1-6}\text{alkyl}$ , wherein the  $C_{1-6}\text{alkyl}$  and  $OC_{1-6}\text{alkyl}$  are linear or branched and optionally substituted with 1 – 5 halogens

(16) OH

(17)  $OR^{1302}$ , and

(18)  $NR^{1305}R^{1306}$ ,

- and  $R^{1301}$  is hydrogen;

-  $R^{1302}$  is  $C_{1-6}\text{alkyl}$ , which is linear or branched and which is unsubstituted or substituted with 1 – 5 groups independently selected from halogen,  $CO_2H$ , and  $CO_2C_{1-6}\text{alkyl}$ , wherein the  $C_{1-6}\text{alkyl}$  is linear or branched;

-  $R^{1303}$  is selected from the group consisting of:

(10) hydrogen,

(11)  $C_{1-10}\text{alkyl}$ , which is linear or branched and which is unsubstituted or substituted with one or more substituted selected from:

a) halogen,

b) hydroxy,

c) phenyl, which is unsubstituted or substituted with 1 – 5 substituents independently selected from halogen, OH,  $C_{1-6}\text{alkyl}$ , and  $OC_{1-6}\text{alkyl}$ ,



wherein the C<sub>1-6</sub>alkyl is linear or branched and optionally substituted with 1 – 5 halogens,

d) naphthyl, wherein the naphthyl is optionally substituted with 1 – 5 substituents independently selected from halogen, OH, C<sub>1-6</sub>alkyl, and OC<sub>1-6</sub>alkyl, wherein the C<sub>1-6</sub>alkyl is linear or branched and optionally substituted with 1 – 5 halogens,

e) CO<sub>2</sub>H,

f) CO<sub>2</sub>C<sub>1-6</sub>alkyl,

g) CONR<sup>1305</sup>R<sup>1306</sup>

(12) CN,

(13) phenyl which is unsubstituted or substituted with 1 – 5 substituents independently selected from C<sub>1-6</sub>alkyl, and OC<sub>1-6</sub>alkyl, hydroxy and halogen, wherein the C<sub>1-6</sub>alkyl is linear or branched and optionally substituted with 1 – 5 halogens,

(14) naphthyl which is unsubstituted or substituted with 1 – 5 substituents independently selected from C<sub>1-6</sub>alkyl, and OC<sub>1-6</sub>alkyl, hydroxy and halogen, wherein the C<sub>1-6</sub>alkyl is linear or branched and optionally substituted with 1 – 5 halogens,

(15) CO<sub>2</sub>H,

(16) CO<sub>2</sub>C<sub>1-6</sub>alkyl,

(17) CONR<sup>1305</sup>R<sup>1306</sup>, and

(18) C<sub>3-6</sub>cycloalkyl, which is unsubstituted or substituted with 1 – 5 substituents independently selected from C<sub>1-6</sub>alkyl, and OC<sub>1-6</sub>alkyl, hydroxy and halogen, wherein the C<sub>1-6</sub>alkyl is linear or branched and optionally substituted with 1 – 5 halogens

- R<sup>1305</sup> and R<sup>1306</sup> are independently selected from the group consisting of:

(5) hydrogen,

(6) phenyl, which is unsubstituted or substituted with substituents independently selected from halogen, OH, C<sub>1-6</sub>alkyl, and OC<sub>1-6</sub>alkyl, wherein the C<sub>1-6</sub>alkyl is linear or branched and optionally substituted with 1 – 5 halogens

(7) C<sub>3-6</sub>cycloalkyl, which is unsubstituted or substituted with 1 – 5 substituents independently selected from C<sub>1-6</sub>alkyl, and OC<sub>1-6</sub>alkyl, wherein the C<sub>1-6</sub>alkyl is linear or branched and optionally substituted with 1 – 5 halogens

(8) C<sub>1-6</sub>alkyl, which is linear or branched and which is unsubstituted or substituted with:

a) halogen, or

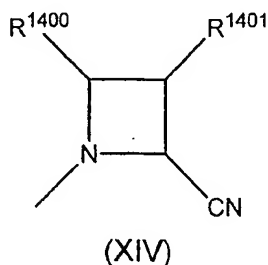
b) phenyl, which is unsubstituted or substituted with 1 – 5 substituents independently selected from halogen, OH, C<sub>1-6</sub>alkyl, and OC<sub>1-6</sub>alkyl, wherein the C<sub>1-6</sub>alkyl is linear or branched and optionally substituted with 1 – 5 halogens,

or wherein R<sup>1305</sup> and R<sup>1306</sup> together with the nitrogen atom to which they are attached form a heterocyclic ring selected from azetidine, pyrrolidine, piperidine, piperazine, and morpholine wherein said heterocyclic ring is unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, C<sub>1-6</sub>alkyl, and C<sub>1-6</sub>alkoxy, wherein alkyl and alkoxy are unsubstituted with one to five halogens;

- R<sup>1304</sup> and R<sup>1307</sup> are hydrogen;

or wherein the group PM

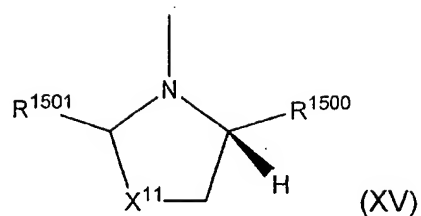
has the formula XIV:



- wherein R<sup>1400</sup> is H and R<sup>1401</sup> is **hydrogen** atom (-H); or halogen, or cyano or ethynyl;

or wherein the group PM

has the formula (XV)

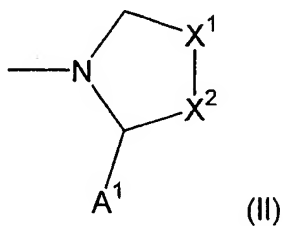


- wherein  $X^{11}$  is  $CH_2$ ,  $CHF$  or  $CF_2$ ;
- wherein  $R^{1500}$  is cyano;
- wherein  $R^{1501}$  is selected from the group consisting of alkyl, alkenyl and alkynyl;

9. Compound according to claims 1, 2, 3, 4, 5, 6, 7, and/or 8

wherein the group PM

has the formula (II)



- wherein  $X^1$  is  $CR^{51}R^{52}$  or S; and
- wherein  $X^2$  is  $CR^{54}R^{55}$ ; and

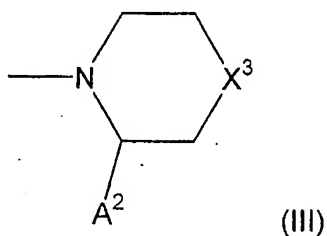
wherein  $R^{51}$ ,  $R^{52}$ ,  $R^{54}$ , and  $R^{55}$ , independently of each other, are a **hydrogen** atom (-H);

wherein  $A^1$  is

- a **hydrogen** atom (-H), or a **boronic acid** group ( $-B(OH)_2$ ), a **cyano** group ( $-C\equiv N$ ), or a **phosphonic acid ester** group ( $-P(=O)(OR^{116})(OR^{117})$ ),
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the pairs  $R^{116}/R^{117}$  may form a part of a **ring**;
- wherein the substituents  $R^{116}$  and  $R^{117}$  independently of each other, are a **hydrogen** atom (-H), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

or wherein the group PM

has the formula (III)



wherein  $X^3$  is  $CR^{131}R^{132}$  or S; and

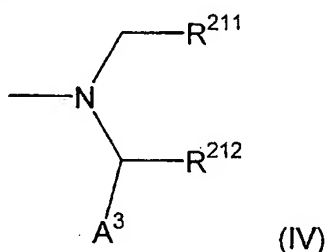
- wherein  $R^{131}$ ,  $R^{132}$ , independently of each other, are a **hydrogen** atom (-H);

wherein  $A^2$  is

- a **hydrogen** atom (-H); a **boronic acid** group (-B(OH)<sub>2</sub>), a **cyano** group (-C≡N), a **phosphonic acid ester** group (-P(=O)(OR<sup>196</sup>)(OR<sup>197</sup>));
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the pairs R<sup>196</sup>/R<sup>197</sup> may form a part of a **ring**; and
- wherein the substituents R<sup>196</sup> and R<sup>197</sup>, independently of each other are a **hydrogen** atom (-H), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

or wherein the group PM

has the formula (IV)



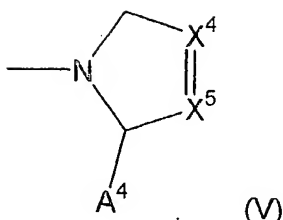
- wherein R<sup>211</sup> and R<sup>212</sup>, independently of each other, are
- a **hydrogen** atom (-H); or a C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, and C<sub>5</sub> branched or straight chain **alkyl**, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, branched or straight chain **alkenyl**, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, branched or straight chain **alkinyl**, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, and C<sub>7</sub> **cycloalkyl**, **aryl**, **heteroaryl**

group or, an **amino** group ( $-\text{NH}_2$ ), or a N-substituted or N,N-disubstituted **amino** group ( $-\text{NHR}^{240}$ ;  $-\text{NR}^{241}\text{R}^{242}$ ); and

- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; and,
- wherein optionally, the pair  $\text{R}^{211}/\text{R}^{212}$ , as well the pairs  $\text{R}^{226}/\text{R}^{227}$ ,  $\text{R}^{230}/\text{R}^{231}$ ,  $\text{R}^{234}/\text{R}^{235}$ ,  $\text{R}^{236}/\text{R}^{237}$  and  $\text{R}^{241}/\text{R}^{242}$ , independently of each other, may form a part of a **ring**; and
- wherein the substituents  $\text{R}^{220}$ ,  $\text{R}^{221}$ ,  $\text{R}^{222}$ ,  $\text{R}^{223}$ ,  $\text{R}^{224}$ ,  $\text{R}^{225}$ ,  $\text{R}^{226}$ ,  $\text{R}^{227}$ ,  $\text{R}^{228}$ ,  $\text{R}^{229}$ ,  $\text{R}^{230}$ ,  $\text{R}^{231}$ ,  $\text{R}^{232}$ ,  $\text{R}^{233}$ ,  $\text{R}^{234}$ ,  $\text{R}^{235}$ ,  $\text{R}^{236}$ ,  $\text{R}^{237}$ ,  $\text{R}^{238}$ ,  $\text{R}^{239}$ ,  $\text{R}^{240}$ ,  $\text{R}^{241}$ , and  $\text{R}^{242}$ , independently of each other, are a **hydrogen** atom ( $-\text{H}$ ), or a  $\text{C}_1$ ,  $\text{C}_2$ ,  $\text{C}_3$ ,  $\text{C}_4$ , and  $\text{C}_5$  branched or straight chain **alkyl**, **aryl**, **heteroaryl**, **amino**, **halo**, **carbonyl**,  $\text{C}_1$ ,  $\text{C}_2$ ,  $\text{C}_3$ ,  $\text{C}_4$ ,  $\text{C}_5$ , branched or straight chain **alkoxy**,  $\text{C}_2$ ,  $\text{C}_3$ ,  $\text{C}_4$ ,  $\text{C}_5$  branched or straight chain **alkenoxy**, **phenyloxy**, **benzyloxy**,  $\text{C}_3$ ,  $\text{C}_4$ ,  $\text{C}_5$  **cycloalkyl**, **cyano**, **amido**, **thiol trifluoromethyl**, or **hydroxy** group; and
- wherein  $\text{A}^3$  is
- a **hydrogen** atom ( $-\text{H}$ ); or a **boronic acid** group ( $-\text{B}(\text{OH})_2$ ), a **cyano** group ( $-\text{C}\equiv\text{N}$ ), or a **phosphonic acid ester** group ( $-\text{P}(=\text{O})(\text{OR}^{276})(\text{OR}^{277})$ )
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; and,
- wherein optionally, the pair  $\text{R}^{276}/\text{R}^{277}$  may form a part of a **ring**; and
- wherein the substituents  $\text{R}^{276}$  and  $\text{R}^{277}$ , independently of each other are a **hydrogen** atom ( $-\text{H}$ ), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

or wherein the group PM

has the formula (V)

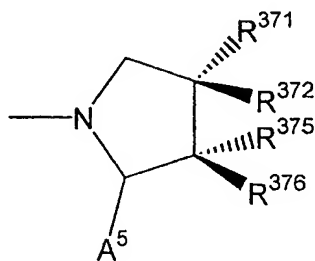


- wherein  $X^4$  is  $CR^{291}$  or N; and
- wherein  $X^5$  is  $CR^{292}$  or N; and
- wherein  $R^{291}$  and  $R^{292}$ , independently of each other, are
- a **hydrogen** atom (-H); or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , and  $C_5$  branched or straight chain **alkyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkenyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkinyl**,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ , and  $C_7$  **cycloalkyl**, **aryl**, **heteroaryl** group or an **amino** group ( $-NH_2$ ), or a N-substituted or N,N-disubstituted **amino** group ( $-NHR^{320}$ ,  $-NR^{321}R^{322}$ ); and
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the **the pair**  $R^{291}/R^{292}$ , if present, as well the pairs  $R^{306}/R^{307}$ ,  $R^{310}/R^{311}$ ,  $R^{314}/R^{315}$ ,  $R^{316}/R^{317}$  and  $R^{321}/R^{322}$ , independently of each other, may form a part of a **ring**; and
- wherein the substituents  $R^{300}$ ,  $R^{301}$ ,  $R^{302}$ ,  $R^{303}$ ,  $R^{304}$ ,  $R^{305}$ ,  $R^{306}$ ,  $R^{307}$ ,  $R^{308}$ ,  $R^{309}$ ,  $R^{310}$ ,  $R^{311}$ ,  $R^{312}$ ,  $R^{313}$ ,  $R^{314}$ ,  $R^{315}$ ,  $R^{316}$ ,  $R^{317}$ ,  $R^{318}$ ,  $R^{319}$ ,  $R^{320}$ ,  $R^{321}$ , and  $R^{322}$ , independently of each other are a **hydrogen** atom (-H), or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , and  $C_5$  branched or straight chain **alkyl**, **aryl**, **heteroaryl**, **amino**, **halo**, **carbonyl**,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkoxy**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  branched or straight chain **alkenoxy**, **phenoxy**, **benzyloxy**,  $C_3$ ,  $C_4$ ,  $C_5$  **cycloalkyl**, **cyano**, **amido**, **thiol** **trifluoromethyl**, or **hydroxy** group; and

- wherein  $A^4$  is
- a **hydrogen** atom (-H); or a **boronic acid** group ( $-B(OH)_2$ ), a **cyano** group ( $-C\equiv N$ ), a **phosphonic acid ester** group ( $-P(=O)(OR^{356})(OR^{357})$ ),
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the pairs  $R^{356}/R^{357}$  may form a part of a ring; and
- wherein the substituents  $R^{356}$  and  $R^{357}$ , independently of each other are a **hydrogen** atom (-H), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

or wherein the group **PM**

has the formula (VI)



(VI)

- wherein  $R^{371}$ ,  $R^{372}$ ,  $R^{375}$  and  $R^{376}$ , independently of each other, a **hydrogen** atom (-H); or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , and  $C_5$  branched or straight chain **alkyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkenyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkinyl**,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ , and  $C_7$  **cycloalkyl**, and **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group or, a **carbaldehyde** ( $-CHO$ ), a **ketone** group ( $-CO-R^{380}$ ), a **boronic acid** group

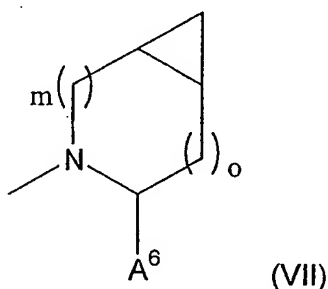


- (-B(OH)<sub>2</sub>), a **cyano** group (-C≡N), a **carboxylic acid** group (-COOH), a **carboxylic acid ester** group (-COOR<sup>381</sup>), a **halogen atom**, a **trifluormethyl** group (-CF<sub>3</sub>), a **thiol** group (-SH); a **thioether** group (-S-R<sup>398</sup>), a **hydroxy** group (-OH); an **alkoxy** group (-O-R<sup>399</sup>), a **tetrazole** group, an **amino** group (-NH<sub>2</sub>), or a **N-substituted or N,N-disubstituted amino** group (-NHR<sup>400</sup>; -NR<sup>401</sup>R<sup>402</sup>); and
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; and,
  - wherein optionally, any **two of the groups** R<sup>371</sup>, R<sup>372</sup>, R<sup>375</sup>, and R<sup>376</sup>, as well as the pairs R<sup>386</sup>/R<sup>387</sup>, R<sup>390</sup>/R<sup>391</sup>, R<sup>394</sup>/R<sup>395</sup>, R<sup>396</sup>/R<sup>397</sup> and R<sup>401</sup>/R<sup>402</sup>, independently of each other, may form a part of a **ring**; and
  - wherein the substituents R<sup>380</sup>, R<sup>381</sup>, R<sup>382</sup>, R<sup>383</sup>, R<sup>384</sup>, R<sup>385</sup>, R<sup>386</sup>, R<sup>387</sup>, R<sup>388</sup>, R<sup>389</sup>, R<sup>390</sup>, R<sup>391</sup>, R<sup>392</sup>, R<sup>393</sup>, R<sup>394</sup>, R<sup>395</sup>, R<sup>396</sup>, R<sup>397</sup>, R<sup>398</sup>, R<sup>399</sup>, R<sup>400</sup>, R<sup>401</sup>, and R<sup>402</sup>, independently of each other are a **hydrogen** atom (-H), or a C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, and C<sub>5</sub> branched or straight chain **alkyl**, **aryl**, **heteroaryl**, **amino**, **halo**, **carbonyl**, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, branched or straight chain **alkoxy**, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> branched or straight chain **alkenoxy**, **phenyloxy**, **benzyloxy**, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> **cycloalkyl**, **cyano**, **amido**, **thiol** **trifluoromethyl**, or **hydroxy** group; and
  - **alternatively**; the two groups R<sup>371</sup> and R<sup>372</sup> can be together an **oxo** (=O) or **hydroxyimino** (=N-OH) group; and
  - **alternatively**; the two groups R<sup>375</sup> and R<sup>376</sup> can be together an **oxo** (=O) or **hydroxyimino** (=N-OH) group; and
  - wherein A<sup>5</sup> is
  - a **hydrogen** atom (-H); or a **boronic acid** group (-B(OH)<sub>2</sub>), a **cyano** group (-C≡N), or a **phosphonic acid ester** group (-P(=O)(OR<sup>436</sup>)(OR<sup>437</sup>));

- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the pairs  $R^{436}/R^{437}$  may form a part of a **ring**; and
- wherein the substituents  $R^{436}$  and  $R^{437}$ , independently of each other are a **hydrogen atom** (-H), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

or wherein the group **PM**

has the formula (VII)

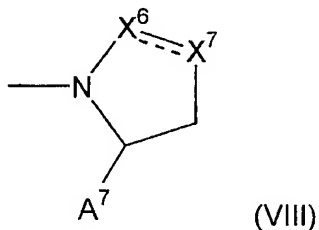


- wherein  $m$  is equal to 0 and  $o$  is equal to 1, or  $m$  is equal to 1 and  $o$  is equal to 0, or  $m$  is equal to 1 and  $o$  is equal to 1, or  $m$  is equal to 2 and  $o$  is equal to 0;
- wherein  $A^6$  is a **hydrogen atom** (-H); or a **boronic acid** group ( $-B(OH)_2$ ), a **cyano** group ( $-C\equiv N$ ), or a **phosphonic acid ester** group ( $-P(=O)(OR^{476})(OR^{477})$ ),
- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the pairs  $R^{476}/R^{477}$  may form a part of a **ring**; and

- wherein the substituents  $R^{476}$  and  $R^{477}$ , independently of each other are a **hydrogen atom (-H)**, or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

or wherein the group PM

has the formula (VIII)



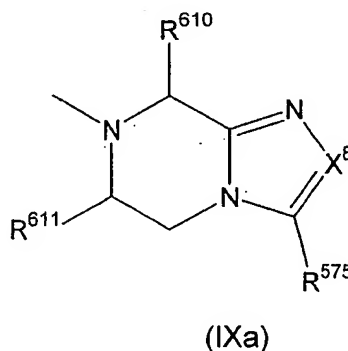
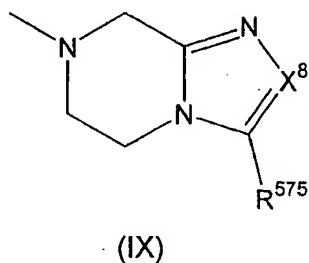
- wherein  $X^6$  is selected from  $CR^{490}R^{491}$ , O, S or  $NR^{492}$ , when the bond between  $X^6$  and  $X^7$  is a single bond; and
- wherein  $X^7$  is selected from  $CR^{493}R^{494}$ , O, S, or  $NR^{495}$ , when the bond between  $X^6$  and  $X^7$  is a single bond;
- **or alternatively,**
- wherein  $X^6$  is selected from  $CR^{496}$  or N, when the bond between  $X^6$  and  $X^7$  is a double bond; and
- wherein  $X^7$  is selected from  $CR^{497}$  or N, when the bond between  $X^6$  and  $X^7$  is a double bond; and
- wherein  $R^{490}$ ,  $R^{491}$ ,  $R^{492}$ ,  $R^{493}$ ,  $R^{494}$ ,  $R^{495}$ ,  $R^{496}$ , and  $R^{497}$ , independently of each other, are a **hydrogen atom (-H)**; or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , and  $C_5$  branched or straight chain **alkyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkenyl**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkinyl**,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$ , and  $C_7$  **cycloalkyl**, **aryl**, **heteroaryl** group, or an **amino** group ( $-NH_2$ ), or a N-substituted or N,N-disubstituted **amino** group ( $-NHR^{520}$ ,  $-NR^{521}R^{522}$ ); and

- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, any two the groups  $R^{490}$ ,  $R^{491}$ ,  $R^{492}$ ,  $R^{493}$ ,  $R^{494}$ ,  $R^{495}$ ,  $R^{496}$ , and  $R^{497}$ , if present, as well as the pairs  $R^{506}/R^{507}$ ,  $R^{510}/R^{511}$ ,  $R^{514}/R^{515}$ ,  $R^{516}/R^{517}$  and  $R^{521}/R^{522}$ , independently of each other, may form a part of a **ring**; **and**
- wherein the substituents  $R^{500}$ ,  $R^{501}$ ,  $R^{502}$ ,  $R^{503}$ ,  $R^{504}$ ,  $R^{505}$ ,  $R^{506}$ ,  $R^{507}$ ,  $R^{508}$ ,  $R^{509}$ ,  $R^{510}$ ,  $R^{511}$ ,  $R^{512}$ ,  $R^{513}$ ,  $R^{514}$ ,  $R^{515}$ ,  $R^{516}$ ,  $R^{517}$ ,  $R^{518}$ ,  $R^{519}$ ,  $R^{520}$ ,  $R^{521}$ , and  $R^{522}$ , independently of each other are a **hydrogen atom (-H)**, or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , and  $C_5$  branched or straight chain **alkyl**, **aryl**, **heteroaryl**, **amino**, **halo**, **carbonyl**,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ , branched or straight chain **alkoxy**,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  branched or straight chain **alkenoxy**, **phenyloxy**, **benzyloxy**,  $C_3$ ,  $C_4$ ,  $C_5$  **cycloalkyl**, **cyano**, **amido**, **thiol trifluoromethyl**, or **hydroxy group**; **and**
- wherein  $A^7$  is
- a **hydrogen atom (-H)**; or a **carbaldehyde (-CHO)**, a **ketone group (-CO- $R^{540}$ )**, a **boronic acid group (-B(OH)<sub>2</sub>)**, a **cyano group (-C≡N)**, a **carboxylic acid group (-COOH)**, a **carboxylic acid ester group (-COOR<sup>541</sup>)**, a **carboxylic acid anhydride group (-CO-O-CO- $R^{542}$ )**, a **hydroxamic acid group (-CO-NH(OH))**, a **N-substituted hydroxamic acid group (-CO-NR<sup>543</sup>(OH))**, a **O-substituted hydroxamic acid group (-CO-NH(OR<sup>544</sup>))**, a **carboxamide group (-CO-NH<sub>2</sub>)**, a **N-substituted or N,N-disubstituted carboxylic acid amide group, (-CO-NHR<sup>545</sup>; -CO-NR<sup>546</sup>R<sup>547</sup>)**, an **amido group (-HN-CO- $R^{548}$ )**, a **sulfonic acid group (-SO<sub>3</sub>H)**, a **sulfonamide group (-SO<sub>2</sub>-NH<sub>2</sub>)**, a **N-substituted or N,N-disubstituted sulfonamide group (-SO<sub>2</sub>-NHR<sup>549</sup>; -SO<sub>2</sub>-NR<sup>550</sup>R<sup>551</sup>)**, an **amidosulfone group (-NH-SO<sub>2</sub>-R<sup>552</sup>)**, a **sulfone group (-SO<sub>2</sub>-R<sup>553</sup>)**, a **phosphoric acid group (-OP(=O)(OH)<sub>2</sub>)**, a **phosphoric acid ester group (-OP(=O)(OR<sup>554</sup>)(OR<sup>555</sup>))**, a **phosphonic acid group (-P(=O)(OH)<sub>2</sub>)**, an **phosphonic acid ester group (-P(=O)(OR<sup>556</sup>)(OR<sup>557</sup>))**, a **halogen atom**, a **trifluormethyl group (-CF<sub>3</sub>)**, a **thiol group (-SH)**; a **thioether group (-S-R<sup>558</sup>)**, a **hydroxy group (-OH)**; an **alkoxy**

group (-O-R<sup>559</sup>), a **tetrazole** group, an **amino** group (-NH<sub>2</sub>), or a N-substituted or N,N-disubstituted **amino** group (-NHR<sup>560</sup>, -NR<sup>561</sup>R<sup>562</sup>); and

- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; and,
- wherein optionally, the pairs R<sup>546</sup>/R<sup>547</sup>, R<sup>550</sup>/R<sup>551</sup>, R<sup>554</sup>/R<sup>555</sup>, R<sup>556</sup>/R<sup>557</sup> and R<sup>561</sup>/R<sup>562</sup>, independently of each other, may form a part of a **ring**; and
- wherein the substituents R<sup>540</sup>, R<sup>541</sup>, R<sup>542</sup>, R<sup>543</sup>, R<sup>544</sup>, R<sup>545</sup>, R<sup>546</sup>, R<sup>547</sup>, R<sup>548</sup>, R<sup>549</sup>, R<sup>550</sup>, R<sup>551</sup>, R<sup>552</sup>, R<sup>553</sup>, R<sup>554</sup>, R<sup>555</sup>, R<sup>556</sup>, R<sup>557</sup>, R<sup>558</sup>, R<sup>559</sup>, R<sup>560</sup>, R<sup>561</sup>, and R<sup>562</sup>, independently of each other are a **hydrogen** atom (-H), or an **alkyl**, **alkenyl**, **alkinyl**, **cycloalkyl**, **cycloalkenyl**, **cycloalkinyl**, **heteroalkyl**, **heteroalkenyl**, **heteroalkinyl**, **heterocycloalkyl**, **heterocycloalkenyl**, **aryl**, **heteroaryl**, **aryl-alkyl**, **heteroaryl-alkyl**, **aryl-heteroalkyl**, **heteroaryl-heteroalkyl** group;

or wherein the group **PM**  
has the formula (IX) or (IXa)



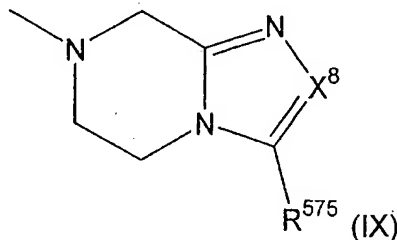
- wherein X<sup>8</sup> is N or CR<sup>570</sup>; and
- wherein R<sup>570</sup>, R<sup>575</sup>, R<sup>610</sup> and R<sup>611</sup> independently of each other, are
- a **hydrogen** atom (-H), a **methyl** group (-CH<sub>3</sub>), a **trifluoromethyl** group (-CF<sub>3</sub>), an **ethyl** group (-C<sub>2</sub>H<sub>5</sub>), a **2,2,2-trifluoroethyl** group (-CH<sub>2</sub>CF<sub>3</sub>), a **pentafluoroethyl** group (-CF<sub>2</sub>CF<sub>3</sub>), a **phenyl** group, (-C<sub>6</sub>H<sub>5</sub>), a **benzyl** group

(-CH<sub>2</sub>-C<sub>6</sub>H<sub>5</sub>), a **benzyloxy** group (-OCH<sub>2</sub>-C<sub>6</sub>H<sub>5</sub>), a **para-ethyl-phenyl** group (-C<sub>6</sub>H<sub>4</sub>-C<sub>2</sub>H<sub>5</sub>), a **para-fluorophenyl** group (-C<sub>6</sub>H<sub>4</sub>-4-F), a **3,4-difluorophenyl** group (-C<sub>6</sub>H<sub>3</sub>-3,4-F<sub>2</sub>), a **para-methoxyphenyl** group (-C<sub>6</sub>H<sub>4</sub>-4-OCH<sub>3</sub>), a **para-trifluoromethoxyphenyl** group (-C<sub>6</sub>H<sub>4</sub>-4-OCF<sub>3</sub>), a **boronic acid** group (-B(OH)<sub>2</sub>), a **cyano** group (-C≡N), a **carboxylic acid** group (-COOH), or a **phosphonic acid ester** group (-P(=O)(OR<sup>596</sup>)(OR<sup>597</sup>));

- which, independently of each other, can be **substituted** with one or more substituents, which can be the same or different; **and**,
- wherein optionally, the pairs R<sup>570</sup>/R<sup>575</sup>, if present, as well as the pair R<sup>596</sup>/R<sup>597</sup>, independently of each other, may form a part of a **ring**; and
- wherein the substituents R<sup>596</sup> and R<sup>597</sup>, independently of each other are a **hydrogen** atom (-H), or a C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, and C<sub>5</sub> branched or straight chain **alkyl**, **aryl**, **heteroaryl**, **amino**, **halo**, **carbonyl**, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, branched or straight chain **alkoxy**, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> branched or straight chain **alkenoxy**, **phenyloxy**, **benzyloxy**, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> **cycloalkyl**, **cyano**, **amido**, **thiol** **trifluoromethyl**, or **hydroxy** group; and

or wherein the group PM

has the formula (IX)

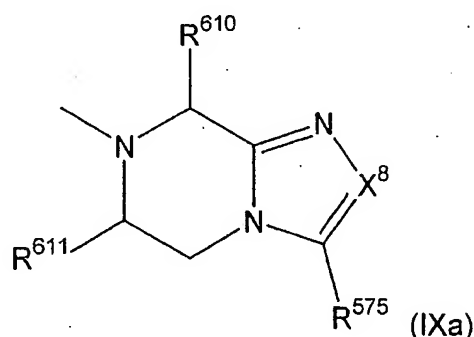


- wherein X<sup>8</sup> is N or CR<sup>570</sup>; and

- wherein  $R^{570}$  and  $R^{575}$ , independently of each other, are
  - (11) hydrogen,
  - (12) CN,
  - (13)  $C_{1-10}$  alkyl, which is linear or branched and which is unsubstituted or substituted with 1-5 halogens or phenyl, which is unsubstituted or substituted with 1-5 substituents independently selected from halogen, CN, OH,  $R^{612}$ ,  $OR^{612}$ ,  $NHSO_2R^{612}$ ,  $SO_2R^{612}$ ,  $CO_2H$ , and  $CO_2C_{1-6}$  alkyl, wherein the  $CO_2C_{1-6}$  alkyl is linear or branched,
  - (14) phenyl which is unsubstituted or substituted with 1-5 substituents independently selected from halogen, CN, OH,  $R^{612}$ ,  $OR^{612}$ ,  $NHSO_2R^{612}$ ,  $SO_2R^{612}$ ,  $CO_2H$ , and  $CO_2C_{1-6}$  alkyl, wherein the  $CO_2C_{1-6}$  alkyl is linear or branched, and
  - (15) a 5- or 6-membered heterocycle which may be saturated or unsaturated comprising 1-4 heteroatoms independently selected from N, S, and O, the heterocycle being unsubstituted or substituted with 1-3 substituents independently selected from oxo, OH, halogen,  $C_{1-6}$  alkyl, and  $OC_{1-6}$  alkyl, wherein  $C_{1-6}$  alkyl and  $C_{1-6}$  alkoxy are linear or branched and optionally substituted with 1-5 halogens, and
- wherein  $R^{612}$  is  $C_{1-6}$  alkyl, which is linear or branched and which is unsubstituted or substituted with 1-5 groups independently selected from halogen,  $CO_2H$ , and  $CO_2C_{1-6}$  alkyl, wherein the  $CO_2C_{1-6}$  alkyl is linear or branched.

or wherein the group PM

has the formula (IXa)



- wherein  $X^8$  is N or  $CR^{570}$ ; and
- wherein  $R^{570}$  and  $R^{575}$  independently of each other, are
  - (16) hydrogen,
  - (17) CN,
  - (18)  $C_{1-10}$  alkyl, which is linear or branched and which is unsubstituted or substituted with 1-5 halogens or phenyl, which is unsubstituted or substituted with 1-5 substituents independently selected from halogen, CN, OH,  $R^{612}$ ,  $OR^{612}$ ,  $NHSO_2R^{612}$ ,  $SO_2R^{612}$ ,  $CO_2H$ , and  $CO_2C_{1-6}$  alkyl, wherein the  $CO_2C_{1-6}$  alkyl is linear or branched,
  - (19) phenyl which is unsubstituted or substituted with 1-5 substituents independently selected from halogen, CN, OH,  $R^{612}$ ,  $OR^{612}$ ,  $NHSO_2R^{612}$ ,  $SO_2R^{612}$ ,  $CO_2H$ , and  $CO_2C_{1-6}$  alkyl, wherein the  $CO_2C_{1-6}$  alkyl is linear or branched, and
  - (20) a 5- or 6-membered heterocycle which may be saturated or unsaturated comprising 1-4 heteroatoms independently selected from N, S, and O, the heterocycle being unsubstituted or substituted with 1-3 substituents independently selected from oxo, OH, halogen,  $C_{1-6}$  alkyl, and  $OC_{1-6}$  alkyl, wherein  $C_{1-6}$  alkyl and  $C_{1-6}$  alkoxy are linear or branched and optionally substituted with 1-5 halogens, and
- wherein  $R^{612}$  is  $C_{1-6}$  alkyl, which is linear or branched and which is unsubstituted or substituted with 1-5 groups independently selected from halogen,  $CO_2H$ , and  $CO_2C_{1-6}$  alkyl, wherein the  $CO_2C_{1-6}$  alkyl is linear or branched, and
- wherein  $R^{610}$  and  $R^{611}$  are each independently selected from the group consisting of
  - (10) hydrogen,
  - (11)  $C_{1-10}$  alkyl, which is linear or branched and which is unsubstituted or substituted with one or more substituents selected from:
    - (a) halogen,
    - (b) hydroxy,
    - (c) phenyl, wherein the phenyl is unsubstituted or substituted with 1-5 substituents independently selected from halogen, OH,  $C_{1-6}$  alkyl,



and C<sub>1-6</sub> alkoxy, wherein the C<sub>1-6</sub> alkyl, and C<sub>1-6</sub> alkoxy are linear or branched and optionally substituted with 1-5 halogens,

(d) naphthyl, wherein the naphthyl is optionally substituted with 1-5 substituents independently selected from halogen, CN, OH, C<sub>1-6</sub> alkyl, and C<sub>1-6</sub> alkoxy, wherein the C<sub>1-6</sub> alkyl, and C<sub>1-6</sub> alkoxy are linear or branched and optionally substituted with 1-5 halogens,

(e) CO<sub>2</sub>H,

(f) CO<sub>2</sub>C<sub>1-6</sub> alkyl,

(g) CONR<sup>613</sup>R<sup>614</sup>, wherein R<sup>613</sup> and R<sup>614</sup> are independently selected from the group consisting of hydrogen, tetrazolyl, phenyl, C<sub>3-6</sub> cycloalkyl and C<sub>1-6</sub> alkyl, wherein the C<sub>1-6</sub> alkyl is linear or branched and is optionally substituted with 1-6 substituents independently selected from 0-5 halogen and 0-1 phenyl, wherein the phenyl or the C<sub>3-6</sub> cycloalkyl being R<sup>613</sup> and R<sup>614</sup> or the optional phenyl substituent on the C<sub>1-6</sub> alkyl are optionally substituted with 1-5 substituents independently selected from halogen, OH, C<sub>1-6</sub> alkyl, and OC<sub>1-6</sub> alkyl, said C<sub>1-6</sub> alkyl and OC<sub>1-6</sub> alkyl being linear or branched and optionally substituted with 1-5 halogens,

or wherein R<sup>613</sup> and R<sup>614</sup> are optionally joined to form a ring selected from pyrrolidine, piperidine or morpholine,

(12) CN,

(13) phenyl, wherein the phenyl is unsubstituted or substituted with 1-5 substituents independently selected from C<sub>1-6</sub> alkyl, and C<sub>1-6</sub> alkoxy, hydroxy and halogen, wherein the C<sub>1-6</sub> alkyl, and C<sub>1-6</sub> alkoxy are linear or branched and optionally substituted with 1-5 halogens,

(14) naphthyl, wherein the naphthyl is unsubstituted or substituted with 1-5 substituents independently selected from halogen, OH, C<sub>1-6</sub> alkyl, and C<sub>1-6</sub> alkoxy, wherein the C<sub>1-6</sub> alkyl, and C<sub>1-6</sub> alkoxy are linear or branched and optionally substituted with 1-5 halogens,

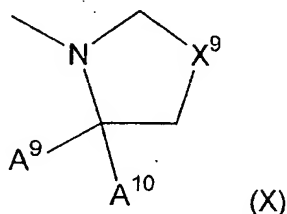
(15) CO<sub>2</sub>H,

(16) CO<sub>2</sub>C<sub>1-6</sub> alkyl,

- (17)  $\text{CONR}^{613}\text{R}^{614}$ , and
- (18)  $\text{C}_{3-6}$  cycloalkyl, which is optionally substituted with 1-5 substituents independently selected from halogen, OH,  $\text{C}_{1-6}$  alkyl, and  $\text{C}_{1-6}$  alkoxy, wherein the  $\text{C}_{1-6}$  alkyl, and  $\text{C}_{1-6}$  alkoxy are linear or branched and optionally substituted with 1-5 halogen, with the proviso that one of  $\text{R}^{610}$  and  $\text{R}^{611}$  is other than hydrogen.

or wherein the group PM

has the formula (X)



- wherein the groups  $\text{X}^9$  is  $\text{CR}^{900}\text{R}^{901}$ , S, SO,  $\text{SO}_2$  or  $\text{NR}^{902}$ 
    - wherein  $\text{R}^{900}$ ,  $\text{R}^{901}$  and  $\text{R}^{902}$ , are, independently of each other, selected from hydrogen, fluorine,  $\text{C}_1$ ,  $\text{C}_2$ ,  $\text{C}_3$ ,  $\text{C}_4$ ,  $\text{C}_5$  or  $\text{C}_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens, or  $-\text{C}(=\text{O})\text{NR}^{910}\text{R}^{911}$ .
  - wherein  $\text{A}^9$  and  $\text{A}^{10}$  are, independently of each other, selected from hydrogen, cyano,  $-\text{C}(=\text{O})\text{NR}^{912}\text{R}^{913}$ , or  $\text{C}_1$ ,  $\text{C}_2$ ,  $\text{C}_3$ ,  $\text{C}_4$ ,  $\text{C}_5$  or  $\text{C}_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens;
- wherein
- $\text{R}^{910}$  and  $\text{R}^{912}$ , are, independently of each other, selected from hydrogen, or  $\text{C}_1$ ,  $\text{C}_2$ ,  $\text{C}_3$ ,  $\text{C}_4$ ,  $\text{C}_5$  or  $\text{C}_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens; and
  - $\text{R}^{911}$  and  $\text{R}^{913}$ , are, independently of each other, selected from the group consisting of

(1) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5, substituents independently selected from halogen and R<sup>920</sup>;

(2) C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6 or 7 substituents independently selected from (a) 0, 1, 2, 3, 4, or 5 halogens, and (b) 0, 1, 2 substituents selected from the group consisting of

- (a) hydroxy,
- (b) -COOH,
- (c) -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester,
- (d) phenyl,
- (e) naphthyl,
- (f) C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl,
- (g) a 5 - or 6 membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur;
- (h) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (a) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (b) a benzene ring fused to a 5- or 6-membered heterocycle having 1, 2, or 3 hetero atoms;

- wherein said C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl, phenyl, naphthyl, are optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from halogen and R<sup>920</sup>, and said 5 or 6 membered heterocycle and said 8, 9 or 10 - membered bicyclic ring system are each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from from oxo, hydroxy, halogen, and R<sup>920</sup>; and

(3) C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, which is optionally substituted with 1, 2, or 3 groups independently selected from halogen, hydroxy, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>,

C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein R<sup>920</sup> is selected from the group consisting of:

- (1) hydroxy;
- (2) cyano;
- (3) C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl optionally substituted with 1, 2, or 3 groups independently selected from halogen, hydroxy, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, wherein said -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl are linear or branched and are optionally substituted with 1, 2, 3, 4, 5 or 6 substituents selected from 1, 2, 3, 4, or 5 halogens, and 0 or 1 substituents selected from -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, -COOH, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl substituents being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;
- (4) C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub>, C<sub>9</sub> or C<sub>10</sub> alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6, or 7 substituents independently selected from 0, 1, 2, 3, 4, or 5 halogen atoms and 0, 1, or 2 groups selected from
  - (a) hydroxy;
  - (b) -COOH;
  - (c) -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, which may linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens;
  - (d) a 5 - or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl,

said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(e) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (i) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (ii) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(f) -CONR<sup>925</sup>R<sup>925</sup>;

(g) -SO<sub>2</sub>NR<sup>925</sup>R<sup>925</sup>;

(h) -NR<sup>925</sup>-C(=O)R<sup>925</sup>

(i) -NR<sup>925</sup>-C(=O)NR<sup>925</sup>R<sup>925</sup>;

(j) -NR<sup>925</sup>COOR<sup>930</sup>

(k) -O-CO-R<sup>930</sup>

(l) -O-CO-NR<sup>925</sup>R<sup>925</sup>;

(m) -NR<sup>925</sup>SO<sub>2</sub>R<sup>930</sup>;

(n) -NR<sup>925</sup>R<sup>925</sup>;

(o) phenyl which is optionally substituted with 1, 2, 3, 4, or 5 group independently selected from halogen, hydroxy, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, 5, or 6 substituents independently selected from 0 or 1 C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl and 0, 1, 2, 3, 4, or 5 halogens, and

- (p) C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, which is optionally substituted with 1, 2, 3, 4, 5, or 6 halogens;
- (5) OC<sub>1</sub>, OC<sub>2</sub>, OC<sub>3</sub>, OC<sub>4</sub>, OC<sub>5</sub>, OC<sub>6</sub>, OC<sub>7</sub>, OC<sub>8</sub>, OC<sub>9</sub> or OC<sub>10</sub> alkyl, which is linear or branched and is optionally substituted with 0, 1, 2, 3, 4, or 5 halogen atoms and 0, 1, or 2 substituents selected from
- (a) hydroxy;
  - (b) -COOH;
  - (c) -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, which may be linear or branched and is optionally substituted with 1, 2, 3, 4 or 5 halogens;
  - (d) a 5 - or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.;
  - (e) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (i) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (ii) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;
  - (f) -CONR<sup>925</sup>R<sup>925</sup>;
  - (g) -SO<sub>2</sub>NR<sup>925</sup>R<sup>925</sup>;
  - (h) -NR<sup>925</sup>-C(=O)R<sup>925</sup>

(i)  $-\text{NR}^{925}-\text{C}(=\text{O})\text{NR}^{925}\text{R}^{925}$ ;

(j)  $-\text{NR}^{925}\text{COOR}^{930}$

(k)  $-\text{O}-\text{CO}-\text{R}^{930}$

(l)  $-\text{O}-\text{CO}-\text{NR}^{925}\text{R}^{925}$ ;

(m)  $-\text{NR}^{925}\text{SO}_2\text{R}^{930}$ ;

(n)  $-\text{NR}^{925}\text{R}^{925}$ ;

(o) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5 groups independently selected from halogen, hydroxy,  $\text{C}_1$ ,  $\text{C}_2$ ,  $\text{C}_3$ ,  $\text{C}_4$ ,  $\text{C}_5$  or  $\text{C}_6$  alkyl,  $-\text{OC}_1$ ,  $-\text{OC}_2$ ,  $-\text{OC}_3$ ,  $-\text{OC}_4$ ,  $-\text{OC}_5$  or  $-\text{OC}_6$  alkyl,  $-\text{COOH}$ ,  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester, said  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  alkyl,  $-\text{OC}_1$ ,  $-\text{OC}_2$ ,  $-\text{OC}_3$ ,  $-\text{OC}_4$ ,  $-\text{OC}_5$  or  $-\text{OC}_6$  alkyl,  $-\text{COOH}$ ,  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, 5, or 6 substituents independently selected from 0 or 1  $\text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  cycloalkyl and 0, 1, 2, 3, 4, or 5 halogens, and

(p)  $\text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  cycloalkyl, which is optionally substituted with 1, 2, 3, 4, 5, or 6 halogens;

(6)  $-\text{COOH}$ ;

(7)  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester, which may be linear or branched and is optionally substituted with 1, 2, 3, 4, 5 halogens;

(8) a 5 - or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, said heterocycle being optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen,  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5$  or  $-\text{OC}_6$  alkyl, said  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5$  or  $-\text{OC}_6$  alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.

(9) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (a) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (b) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused

to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(10) -CONR<sup>925</sup>R<sup>925</sup>;

(11) -SO<sub>2</sub>NR<sup>925</sup>R<sup>925</sup>;

(12) -NR<sup>925</sup>-C(=O)R<sup>925</sup>

(13) -NR<sup>925</sup>-C(=O)NR<sup>925</sup>R<sup>925</sup>;

(14) -NR<sup>925</sup>COOR<sup>930</sup>

(15) -O-CO-R<sup>930</sup>

(16) -O-CO-NR<sup>925</sup>R<sup>925</sup>;

(17) -NR<sup>925</sup>SO<sub>2</sub>R<sup>930</sup>;

(18) -NR<sup>925</sup>R<sup>925</sup>;

(19) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5 group independently selected from halogen, hydroxy, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein R<sup>930</sup> is selected from the group consisting of phenyl, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl, and C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl, wherein C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6, substituents independently selected from 0, 1, 2, 3, 4, or 5 halogens, 0 or 1 phenyl, wherein said optional phenyl substituent and said R<sup>930</sup>, when R<sup>930</sup> is phenyl or C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl, are optionally substituted with 1, 2, 3, 4, or 5 substituents, independently selected from halogen, OH, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, or C<sub>5</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, or -OC<sub>5</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, or C<sub>5</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, or -OC<sub>5</sub>

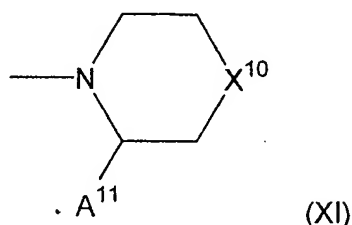


alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.

wherein  $R^{925}$  is selected from  $R^{930}$  and hydrogen.

wherein the group PM

has the formula (XI)



- wherein the groups  $X^{10}$  is  $CR^{1000}R^{1001}$ , S,  $SO$ ,  $SO_2$  or  $NR^{1002}$ 
  - wherein  $R^{1000}$ ,  $R^{1001}$  and  $R^{1002}$ , are, independently of each other, selected from hydrogen, fluorine,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens, or  $-C(=O)NR^{1010}R^{1011}$ .

and  $A^{11}$  is selected from

hydrogen, cyano,  $-C(=O)NR^{1012}R^{1013}$ , or  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein

- $R^{1010}$  and  $R^{1012}$ , are, independently of each other, selected from hydrogen, or  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens; and
- $R^{1011}$  and  $R^{1013}$ , are, independently of each other, selected from the group consisting of

(1) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5, substituents independently selected from halogen and  $R^{1020}$ ;

(2) C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6 or 7 substituents independently selected from (a) 0, 1, 2, 3, 4, or 5 halogens, and (b) 0, 1, 2 substituents selected from the group consisting of

- (a) hydroxy,
- (b) -COOH,
- (c) -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester,
- (d) phenyl,
- (e) naphthyl,
- (f) C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl,
- (g) a 5 - or 6 membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur;
- (h) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (a) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (b) a benzene ring fused to a 5- or 6-membered heterocycle having 1, 2, or 3 hetero atoms;

- wherein said C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl, phenyl, naphthyl, are optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from halogen and R<sup>1020</sup>, and said 5 or 6 membered heterocycle and said 8, 9 or 10 - membered bicyclic ring system are each optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, and R<sup>1020</sup>; and

(3) C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl, which is optionally substituted with 1, 2, or 3 groups independently selected from halogen, hydroxy, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

wherein R<sup>1020</sup> is selected from the group consisting of:

- (1) hydroxy;
- (2) cyano;

(3) C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl optionally substituted with 1, 2, or 3 groups independently selected from halogen, hydroxy, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl), i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, wherein said -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl are linear or branched and are optionally substituted with 1, 2, 3, 4, 5 or 6 substituents selected from 1, 2, 3, 4, or 5 halogens, and 0 or 1 substituents selected from -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, -COOH, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl substituents being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(4) C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub>, C<sub>6</sub>, C<sub>7</sub>, C<sub>8</sub>, C<sub>9</sub> or C<sub>10</sub> alkyl, which is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6, or 7 substituents independently selected from 0, 1, 2, 3, 4, or 5 halogen atoms and 0, 1, or 2 groups selected from

(a) hydroxy;

(b) -COOH;

(c) -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, which may linear or branched and is optionally substituted with 1, 2, 3, 4, or 5 halogens;

(d) a 5 - or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.;

(e) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (i) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (ii) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being

linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(f)  $-\text{CONR}^{1025}\text{R}^{1025}$ ;

(g)  $-\text{SO}_2\text{NR}^{1025}\text{R}^{1025}$ ;

(h)  $-\text{NR}^{1025}-\text{C}(=\text{O})\text{R}^{1025}$

(i)  $-\text{NR}^{1025}-\text{C}(=\text{O})\text{NR}^{1025}\text{R}^{1025}$ ;

(j)  $-\text{NR}^{1025}\text{COOR}^{1030}$

(k)  $-\text{O}-\text{CO}-\text{R}^{1030}$

(l)  $-\text{O}-\text{CO}-\text{NR}^{1025}\text{R}^{1025}$ ;

(m)  $-\text{NR}^{1025}\text{SO}_2\text{R}^{1030}$ ;

(n)  $-\text{NR}^{1025}\text{R}^{1025}$ ;

(o) phenyl which is optionally substituted with 1, 2, 3, 4, or 5 group independently selected from halogen, hydroxy,  $\text{C}_1$ ,  $\text{C}_2$ ,  $\text{C}_3$ ,  $\text{C}_4$ ,  $\text{C}_5$  or  $\text{C}_6$  alkyl,  $-\text{OC}_1$ ,  $-\text{OC}_2$ ,  $-\text{OC}_3$ ,  $-\text{OC}_4$ ,  $-\text{OC}_5$  or  $-\text{OC}_6$  alkyl,  $-\text{COOH}$ ,  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester, said  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  alkyl,  $-\text{OC}_1$ ,  $-\text{OC}_2$ ,  $-\text{OC}_3$ ,  $-\text{OC}_4$ ,  $-\text{OC}_5$  or  $-\text{OC}_6$  alkyl,  $-\text{COOH}$ ,  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, 5, or 6 substituents independently selected from 0 or 1  $\text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  cycloalkyl and 0, 1, 2, 3, 4, or 5 halogens, and

(p)  $\text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  cycloalkyl, which is optionally substituted with 1, 2, 3, 4, 5, or 6 halogens;

(5)  $\text{OC}_1, \text{OC}_2, \text{OC}_3, \text{OC}_4, \text{OC}_5, \text{OC}_6, \text{OC}_7, \text{OC}_8, \text{OC}_9$  or  $\text{OC}_{10}$  alkyl, which is linear or branched and is optionally substituted with 0, 1, 2, 3, 4, or 5 halogen atoms and 0, 1, or 2 substituents selected from

(a) hydroxy;

(b)  $-\text{COOH}$ ;

(c)  $-\text{COO}(\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5 \text{ or } \text{C}_6 \text{ alkyl})$  i.e. ester, which may be linear or branched and is optionally substituted with 1, 2, 3, 4 or 5 halogens;

(d) a 5 - or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, optionally substituted with 1, 2, or 3 substituents independently selected from oxo, hydroxy, halogen,  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5$  or  $-\text{OC}_6$  alkyl, said  $\text{C}_1, \text{C}_2, \text{C}_3, \text{C}_4, \text{C}_5$  or  $\text{C}_6$  alkyl, and  $-\text{OC}_1, -\text{OC}_2, -\text{OC}_3, -\text{OC}_4, -\text{OC}_5$  or  $-\text{OC}_6$  alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.;

(e) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (i) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (ii) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(f) -CONR<sup>1025</sup>R<sup>1025</sup>;

(g) -SO<sub>2</sub>NR<sup>1025</sup>R<sup>1025</sup>;

(h) -NR<sup>1025</sup>-C(=O)R<sup>1025</sup>

(i) -NR<sup>1025</sup>-C(=O)NR<sup>1025</sup>R<sup>1025</sup>;

(j) -NR<sup>1025</sup>COOR<sup>1030</sup>

(k) -O-CO-R<sup>1030</sup>

(l) -O-CO-NR<sup>1025</sup>R<sup>1025</sup>;

(m) -NR<sup>1025</sup>SO<sub>2</sub>R<sup>1030</sup>;

(n) -NR<sup>1025</sup>R<sup>1025</sup>;

(o) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5 groups independently selected from halogen, hydroxy, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, 5, or 6 substituents independently selected from 0 or 1 C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl and 0, 1, 2, 3, 4, or 5 halogens, and

(p) C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> cycloalkyl, which is optionally substituted with 1, 2, 3, 4, 5, or 6 halogens;

(6) -COOH;

(7) -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, which may be linear or branched and is optionally substituted with 1, 2, 3, 4, 5 halogens;

(8) a 5- or 6-membered heterocycle which may be saturated or unsaturated comprising 1, 2, 3, or 4 hetero atoms independently selected from nitrogen, oxygen and sulfur, said heterocycle being optionally substituted with 1, 2, or

3 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens.

(9) an 8, 9 or 10 membered bicyclic ring system which may be saturated or unsaturated comprising (a) two fused heterocyclic rings, each heterocyclic ring having 1, 2, 3, or 4 heteroatoms independently selected from nitrogen, oxygen or sulfur, or (b) a 5- or 6-membered heterocycle having 1, 2, or 3 heteroatoms independently selected from nitrogen, oxygen and sulfur, fused to a benzene ring, wherein said bicyclic ring system is optionally substituted with 1, 2, 3, 4, or 5 substituents independently selected from oxo, hydroxy, halogen, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, and -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

(10) -CONR<sup>1025</sup>R<sup>1025</sup>,

(11) -SO<sub>2</sub>NR<sup>1025</sup>R<sup>1025</sup>,

(12) -NR<sup>1025</sup>-C(=O)R<sup>1025</sup>

(13) -NR<sup>1025</sup>-C(=O)NR<sup>1025</sup>R<sup>1025</sup>,

(14) -NR<sup>925</sup>COOR<sup>1030</sup>

(15) -O-CO-R<sup>1030</sup>

(16) -O-CO-NR<sup>1025</sup>R<sup>1025</sup>,

(17) -NR<sup>1025</sup>SO<sub>2</sub>R<sup>1030</sup>,

(18) -NR<sup>1025</sup>R<sup>1025</sup>,

(19) phenyl, which is optionally substituted with 1, 2, 3, 4, or 5 group independently selected from halogen, hydroxy, C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester, said C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, -OC<sub>1</sub>, -OC<sub>2</sub>, -OC<sub>3</sub>, -OC<sub>4</sub>, -OC<sub>5</sub> or -OC<sub>6</sub> alkyl, -COOH, -COO(C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl) i.e. ester being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens;

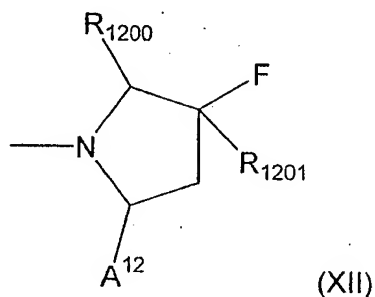
wherein R<sup>1030</sup> is selected from the group consisting of phenyl, C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, and C<sub>3</sub>, C<sub>4</sub> C<sub>5</sub> or C<sub>6</sub> cycloalkyl, wherein C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl is linear or branched and is optionally substituted with 1, 2, 3, 4, 5, 6, substituents independently selected from 0, 1, 2, 3, 4, or 5

halogens, 0 or 1 phenyl, wherein said optional phenyl substituent and said  $R^{930}$ , when  $R^{930}$  is phenyl or  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  cycloalkyl, are optionally substituted with 1, 2, 3, 4, or 5 substituents, independently selected from halogen, OH,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , or  $C_5$  alkyl,  $-OC_1$ ,  $-OC_2$ ,  $-OC_3$ ,  $-OC_4$ , or  $-OC_5$  alkyl, said  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , or  $C_5$  alkyl,  $-OC_1$ ,  $-OC_2$ ,  $-OC_3$ ,  $-OC_4$ , or  $-OC_5$  alkyl being linear or branched and optionally substituted with 1, 2, 3, 4, or 5 halogens,

wherein  $R^{1025}$  is selected from  $R^{1030}$  and hydrogen.

or wherein the group PM

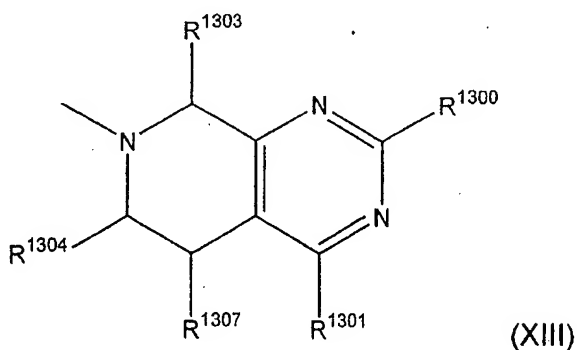
has the formula (XII)



- wherein the groups  $R^{1201}$  is hydrogen or fluoro.
- wherein  $R^{1200}$  and  $A^{12}$  is selected from hydrogen and cyano, and the other is hydrogen.

or wherein the group PM

has the formula XIII:



wherein:

-  $R^{1300}$  is selected from the group consisting of:

- (10) hydrogen,
- (11) CN,
- (12)  $C_{1-10}$ alkyl, which is linear or branched which is unsubstituted or substituted with:
  - a) halogen, or
  - b) phenyl, which is unsubstituted or substituted with 1 - 5 substituents independently selected from halogen, CN, OH,  $R^{1302}$ ,  $OR^{1302}$ ,  $NHSO_2R^{1302}$ ,  $N(C_{1-6}alkyl)SO_2R^{1302}$ ,  $SO_2R^{1302}$ ,  $SO_2NR^{1305}R^{1306}$ ,  $NR^{1305}R^{1306}$ ,  $CONR^{1305}R^{1306}$ ,  $CO_2H$ , and  $CO_2C_{1-6}alkyl$ , wherein the  $C_{1-6}alkyl$  is linear or branched,
- (13) phenyl which is unsubstituted or substituted with 1 - 5 substituents independently selected from halogen, CN, OH,  $R^{1302}$ ,  $OR^{1302}$ ,  $NHSO_2R^{1302}$ ,  $N(C_{1-6}alkyl)SO_2R^{1302}$ ,  $SO_2R^{1302}$ ,  $SO_2NR^{1305}R^{1306}$ ,  $NR^{1305}R^{1306}$ ,  $CONR^{1305}R^{1306}$ ,  $CO_2H$ , and  $CO_2C_{1-6}alkyl$ , wherein the  $C_{1-6}alkyl$  is linear or branched,
- (14) a 5- or 6-membered heterocyclic which may be saturated or unsaturated comprising 1 - 4 heteroatoms independently selected from N, S and O, the heterocycle being unsubstituted or substituted with 1 - 3 substituents independently selected from oxo, halogen,  $NO_2$ , CN, OH,  $R^{1302}$ ,  $OR^{1302}$ ,  $NHSO_2R^{1302}$ ,  $N(C_{1-6}alkyl)SO_2R^{1302}$ ,  $SO_2R^{1302}$ ,  $SO_2NR^{1305}R^{1306}$ ,  $NR^{1305}R^{1306}$ ,  $CONR^{1305}R^{1306}$ ,  $CO_2H$ , and  $CO_2C_{1-6}alkyl$ , wherein the  $C_{1-6}alkyl$  is linear or branched,
- (15)  $C_{3-6}$ cycloalkyl, which is optionally substituted with 1 - 5 substituents independently selected from halogen, OH,  $C_{1-6}alkyl$ , and  $OC_{1-6}alkyl$ , wherein the  $C_{1-6}alkyl$  and  $OC_{1-6}alkyl$  are linear or branched and optionally substituted with 1 - 5 halogens,
- (16) OH,
- (17)  $OR^{1302}$ , and
- (18)  $NR^{1305}R^{1306}$ ,

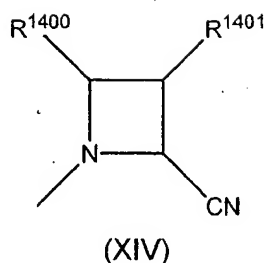


- R<sup>1301</sup> is hydrogen;
  - R<sup>1302</sup> is C<sub>1-6</sub>alkyl, which is linear or branched and which is unsubstituted or substituted with 1 – 5 groups independently selected from halogen, CO<sub>2</sub>H, and CO<sub>2</sub>C<sub>1-6</sub>alkyl, wherein the C<sub>1-6</sub>alkyl is linear or branched;
  - R<sup>1303</sup> is hydrogen;
  - R<sup>1305</sup> and R<sup>1306</sup> are independently selected from the group consisting of:
    - (5) hydrogen,
    - (6) phenyl, which is unsubstituted or substituted with substituents independently selected from halogen, OH, C<sub>1-6</sub>alkyl, and OC<sub>1-6</sub>alkyl, wherein the C<sub>1-6</sub>alkyl is linear or branched and optionally substituted with 1 – 5 halogens
    - (7) C<sub>3-6</sub>cycloalkyl; which is unsubstituted or substituted with 1 – 5 substituents independently selected from C<sub>1-6</sub>alkyl, and OC<sub>1-6</sub>alkyl, wherein the C<sub>1-6</sub>alkyl is linear or branched and optionally substituted with 1 – 5 halogens
    - (8) C<sub>1-6</sub>alkyl, which is linear or branched and which is unsubstituted or substituted with:
      - a) halogen, or
      - b) phenyl, which is unsubstituted or substituted with 1 – 5 substituents independently selected from halogen, OH, C<sub>1-6</sub>alkyl, and OC<sub>1-6</sub>alkyl, wherein the C<sub>1-6</sub>alkyl is linear or branched and optionally substituted with 1 – 5 halogens,
- or wherein R<sup>1305</sup> and R<sup>1306</sup> together with the nitrogen atom to which they are attached form a heterocyclic ring selected from azetidine, pyrrolidine, piperidine, piperazine, and morpholine wherein said heterocyclic ring is unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, C<sub>1-6</sub>alkyl, and C<sub>1-6</sub>alkoxy, wherein alkyl and alkoxy are unsubstituted with one to five halogens;

-  $R^{1304}$  and  $R^{1307}$  are hydrogen;

or wherein the group PM

has the formula XIV:



- wherein  $R^{1400}$  is H and  $R^{1401}$  is hydrogen atom (-H); or fluoro, or cyano.

10. A composition comprising a compound according to any one of the preceding claims in combination with acarbose.
11. A composition comprising a compound according to any one of the claims 1 to 9 in combination with metformin.
12. A composition comprising a compound according to any one of the claims 1 to 9 in combination with acarbose and metformin.
13. A composition comprising a compound according to any one of the claims 1 to 9 in combination with
- (a) other DP IV inhibitors
  - (b) insulin sensitizers selected from the group consisting of
    - (i) PPAR agonists,
    - (ii) biguanides, and
    - (iii) protein tyrosin phosphatase-1B (PTP-1B) inhibitors;

- (c) insulin and insulin mimetics;
- (d) sulfonylureas and other insulin secretagogues;
- (e)  $\alpha$ -glucosidase inhibitors;
- (f) glucagon receptor agonists;
- (g) GLP-1; GLP-1 mimetics, e.g. NN-2211 (liraglutide from Novo Nordisk), and GLP-1 receptor agonists;
- (h) GLP-2; GLP-2 mimetics, e.g. ALX-0600 (teduglutide from NPS Allelix Corp.) and GLP-2 receptor agonists;
- (i) exendin-4 and exendin-4 mimetics, e.g. exenatide (AC-2993, synthetic exendin-4 from Amylin/Eli Lilly);
- (j) GIP, GIP mimetics, and GIP receptor agonists;
- (k) PACAP, PACAP mimetics, and PACAP receptor 3 agonists;
- (l) cholesteral lowering agents selected from the group consisting of
  - (i) HMG-CoA reductase inhibitors,
  - (ii) sequestrants,
  - (iii) nicotinic alcohol, nicotinic acid and salts thereof,
  - (iv) PPAR $\alpha$  agonists,
  - (v) PPAR $\alpha/\gamma$  dual agonists,
  - (vi) inhibitors of cholesterol absorption,
  - (vii) acyl CoA:cholesterol acyltransferase inhibitors, and
  - (viii) antioxidants;
- (m) PPAR $\delta$  agonists;
- (n) antiobesity compounds;
- (o) an ileal bile acid transporter inhibitor; and
- (p) anti-inflammatory agents.

14. A composition comprising a compound according to any one of the claims 1 to 9 in combination with a gene therapeutic expression system for GLP-1 comprising a viral vector comprising

- (a) a polynucleotide sequence encoding GLP-1 (glucagon like peptide - 1); and

- (b) a polynucleotide sequence encoding a signal sequence upstream of (a);  
and
  - (c) a polyadenylation signal downstream of (a); and
  - (d) a polynucleotide sequence encoding a proteolytic cleavage site located between the polynucleotide sequence encoding GLP-1 and the polynucleotide sequence encoding the signal sequence; and
  - (e) wherein the expression of GLP-1 underlies a constitutive promoter or is controlled by a regulatable promoter;
  - (f) wherein, optionally, the viral vector comprises a polynucleotide sequence encoding GIP (glucose dependent insulinotropic peptide);
  - (g) *wherein, optionally, the viral vector is encompassed by a mammalian cell.*
15. A composition comprising a compound according to any one of the claims 1 to 9 in combination with a gene therapeutic expression system for GIP comprising a viral vector comprising
- (a) a polynucleotide sequence encoding GIP (glucose dependent insulinotropic peptide); and
  - (b) a polynucleotide sequence encoding a signal sequence upstream of (a);  
and
  - (c) a polyadenylation signal downstream of (a); and
  - (d) a polynucleotide sequence encoding a proteolytic cleavage site located between the polynucleotide sequence encoding GIP and the polynucleotide sequence encoding the signal sequence; and
  - (e) wherein the expression of GIP underlies a constitutive promoter or is controlled by a regulatable promoter;
  - (f) wherein, optionally, the viral vector comprises a polynucleotide sequence encoding GLP-1 (glucagon like peptide 1);
  - (g) *wherein, optionally, the viral vector is encompassed by a mammalian cell.*

16. A composition comprising a compound according to any one of the claims 1 to 9 in combination with a gene therapeutic expression system for GLP-1 and / or GIP wherein

- the signal sequence upstream of the gene of interest (GLP-1; GIP) is the murine immunoglobulin  $\kappa$  signal sequence or the glia monster exendin signal sequence; and / or
- the polyadenylation signal downstream of the gene of interest (GLP-1; GIP) is derived from simian virus 40 (SV 40); and /or
- the proteolytic cleavage site is cleaved by furin pretease; and/ or
- the gene delivery vector for expression the gene of interest is an adenoviral, retroviral, leniviral, adeno associated viral vector; and /or
- the constitutive promoter is a cytomegalovirus (CMV) promotor, or a Rous sarcoma long-terminal repeat (LTR) sequence, and the SV 40 early gene gene promoter; and the inducible promoter is the Tet-On<sup>TM</sup> / Tet-Off<sup>TM</sup> system available from Clontech; and /or
- the mammalian cell is a primate or rodent cell, preferably a human cell, more preferably a human hepatocyte.

17. A composition according to any one of the claims 11 to 16, which additionally comprises an inhibitor of glutaminyl cyclase.

18. A Pharmaceutical composition comprising a compound or composition according to any one of the preceding claims, and optionally a pharmaceutical acceptable diluent and/or carrier.

19. Use of a composition or a pharmaceutical composition according to any one of the claims 11 to 18 for the preparation of a medicament for the inhibition of dipeptidyl peptidase IV and dipeptidyl peptidase IV – like enzyme activity in a mammal.

20. Use of a composition or a pharmaceutical composition according to any one of the claims 11 to 18 for the preparation of a medicament for the treatment of disorders

related to the inhibition of dipeptidyl peptidase IV dipeptidyl peptidase IV – like enzyme activity in a mammal.

21. The use according to claims 19 or 20 for the preparation of a medicament for the treatment of indications selected from the group consisting of non-insulin dependent diabetes mellitus (type 2), impaired glucose tolerance, impaired fasting glucose, impaired glucose metabolism, prediabetes, glucosuria, and disturbances of signal action at the cells of the islets of Langerhans and insulin sensitivity in the peripheral tissue in the postprandial phase of mammals, insulin resistance, lipid disorders, hyperlipidemia, metabolic acidosis, diabetic neuropathy and nephropathy and of sequelae caused by diabetes mellitus in mammals; obesity, metabolism-related hypertension and cardiovascular sequelae caused by hypertension in mammals; atherosclerosis and its sequelae, inflammatory bowel disease, including Crohn's disease and ulcerative colitis, other inflammatory conditions, pancreatitis, tumor metastasis, benign prostatic hypertrophy, gingivitis, osteoporosis, for the prophylaxis or treatment of skin diseases and diseases of the mucosae, autoimmune diseases and inflammatory conditions, and for the prophylaxis or treatment of psychosomatic, neuropsychiatric and depressive illness, and neurodegenerative diseases such as anxiety, depression, sleep disorders, chronic fatigue, schizophrenia, epilepsy, nutritional disorders, spasm, and chronic pain.

22. The use according to any one of the claims 19 to 21 for the preparation of a medicament for the treatment of indications selected from the group consisting of non-insulin dependent diabetes mellitus (type 2), prediabetes, impaired glucose tolerance, impaired fasting glucose and impaired glucose metabolism.

23. A method for the inhibition of dipeptidyl peptidase IV and dipeptidyl peptidase IV – like enzyme activity in a mammal comprising the step of administering to a mammal a therapeutically effective amount of a composition or a pharmaceutical composition according to any one of the claims 11 to 18.

24. The method according to claim 23 for the treatment of disorders related to the inhibition of dipeptidyl peptidase IV dipeptidyl peptidase IV – like enzyme activity.

25. The method according to claim 24 for the treatment of indications selected from the group consisting of non-insulin dependent diabetes mellitus (type 2), impaired glucose tolerance, impaired fasting glucose, impaired glucose metabolism, prediabetes, glucosuria, and disturbances of signal action at the cells of the islets of Langerhans and insulin sensitivity in the peripheral tissue in the postprandial phase of mammals, insulin resistance, lipid disorders, hyperlipidemia, metabolic acidosis, diabetic neuropathy and nephropathy and of sequelae caused by diabetes mellitus in mammals; obesity, metabolism-related hypertension and cardiovascular sequelae caused by hypertension in mammals; atherosclerosis and its sequelae, inflammatory bowel disease, including Crohn's disease and ulcerative colitis, other inflammatory conditions, pancreatitis, tumor metastasis, benign prostatic hypertrophy, gingivitis, osteoporosis, for the prophylaxis or treatment of skin diseases and diseases of the mucosae, autoimmune diseases and inflammatory conditions, and for the prophylaxis or treatment of psychosomatic, neuropsychiatric and depressive illness, and neurodegenerative diseases such as anxiety, depression, sleep disorders, chronic fatigue, schizophrenia, epilepsy, nutritional disorders, spasm, and chronic pain.

26. The method according to claim 25 for the treatment of indications selected from the group consisting of non-insulin dependent diabetes mellitus (type 2), prediabetes, impaired glucose tolerance, impaired fasting glucose and impaired glucose metabolism.